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Dermira, Inc.  
Form 10-K  
February 26, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 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, 2018

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT  
OF 1934  
Commission File Number 001 36668

DERMIRA, INC.

(Exact name of Registrant as specified in its charter)

Delaware 27 3267680  
(State or other jurisdiction of (I.R.S. Employer  
incorporation or organization) Identification No.)

275 Middlefield Road, Suite 150

Menlo Park, CA 94025

(Address of principal executive offices) (Zip Code)

(650) 421 7200

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(Registrant's telephone number, including area code)

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

Title of Each Class:	Name of Each Exchange on which Registered
Common Stock, par value \$0.001 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 Section 15(d) of the Act. Yes No

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

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§232.405 of this chapter) 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, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act:

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

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

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

As of June 29, 2018, the last business day of the Registrant's most recently completed second fiscal quarter, the aggregate market value of common stock held by non-affiliates of the Registrant was approximately \$318,291,176 (based on a closing price of \$9.20 per share as reported by The Nasdaq Global Select Market on June 29, 2018). For

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purposes of this calculation, shares of common stock beneficially owned by the Registrant's officers, directors and certain stockholders as of June 29, 2018 have been excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes. The Registrant has no non-voting common equity.

As of February 19, 2019, the number of outstanding shares of the Registrant's common stock, par value \$0.001 per share, was 42,328,167.

### DOCUMENTS INCORPORATED BY REFERENCE

Certain sections of the Registrant's definitive Proxy Statement to be filed in connection with the Registrant's 2019 Annual Meeting of Stockholders are incorporated by reference into Part III of this Form 10-K where indicated. The Proxy Statement will be filed with the Securities and Exchange Commission pursuant to Regulation 14A within 120 days of the Registrant's fiscal year ended December 31, 2018. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

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Dermira, Inc.

Form 10 K

For the Fiscal Year Ended December 31, 2018

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Unless the context indicates otherwise, as used in this report, the terms “Company,” “Dermira,” “Registrant,” “we,” “us” and “refer to Dermira, Inc., a Delaware corporation, and its sole subsidiary taken as a whole.

“Dermira” is a registered trademark in Australia, Canada, the European Union, Japan, Mexico, Switzerland and the United States. “Dermira” and logo and “D” and logo are registered trademarks in China, the European Union, Hong Kong, Japan and Mexico and are pending trademark applications in Canada and the United States. “Qbrexza” is a

registered trademark in Japan, Mexico and the United States and is a pending trademark application in Canada, China, European Union, Hong Kong and South Korea. All other service marks, trademarks and tradenames appearing in this Annual Report on Form 10 K are the property of their respective owners. Solely for convenience, the trademarks and tradenames referred to in this Annual Report on Form 10 K appear without the® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and tradenames.

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SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

This Annual Report on Form 10 K, including the sections titled “Business,” “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” contains forward looking statements. All statements contained in this Annual Report on Form 10 K other than statements of historical fact, including statements regarding our future consolidated results of operations and financial position, our business strategy and plans, market growth, and our objectives for future operations, are forward looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases, you can identify these statements by forward looking words, such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “could,” “would,” “project,” “plan,” “potential,” “seek” the negative or plural of these words or similar expressions.

These forward looking statements are subject to a number of risks, uncertainties and assumptions, including those described in “Risk Factors” and elsewhere in this Annual Report on Form 10 K. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward looking statements we may make. In light of these risks, uncertainties and assumptions, the forward looking events and circumstances discussed in this report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward looking statements.

You should not rely upon forward looking statements as predictions of future events. Although we believe that the expectations reflected in the forward looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward looking statements will be achieved or occur. Such forward looking statements speak only as of the date of this Annual Report on Form 10 K. Except as may be required by law, we undertake no obligation to update publicly any forward looking statements for any reason after the date of this report to conform these statements to actual results or to changes in our expectations.

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PART I

ITEM 1. BUSINESS

Overview

We are a biopharmaceutical company dedicated to bringing biotech ingenuity to medical dermatology by delivering differentiated, new therapies to the millions of patients living with chronic skin conditions. We are committed to understanding the needs of both patients and physicians and using our insight to identify, develop and commercialize leading-edge medical dermatology products. Our approved treatment, QBREXZA™ (glycopyrronium) cloth (“QBREXZA”), is indicated for pediatric and adult patients (ages nine and older) with primary axillary hyperhidrosis (excessive underarm sweating). We are also evaluating lebrikizumab in a Phase 2b clinical trial for the treatment of moderate-to-severe atopic dermatitis (a severe form of eczema) and have early-stage research and development programs in other areas of dermatology. We are headquartered in Menlo Park, California.

We are focused on the development of therapeutic solutions in medical dermatology to treat skin conditions, such as hyperhidrosis and atopic dermatitis. These diseases impact millions of people worldwide and can have significant, multidimensional effects on patients’ quality of life, including their physical, functional and emotional well being. According to multiple published studies, patients report that medical dermatology conditions affect quality of life in ways comparable to other serious diseases, such as cancer, heart disease, diabetes, epilepsy, asthma and arthritis.

Our portfolio consists of:

QBREXZA, a topical, once-daily anticholinergic cloth that was approved by the U.S. Food and Drug Administration (“FDA”) in June 2018 for the treatment of primary axillary hyperhidrosis in adult and pediatric patients nine years of age and older. Primary axillary hyperhidrosis is a medical condition with no known cause that results in underarm sweating beyond what is needed for normal body temperature regulation. Anticholinergics are a class of pharmaceutical products that exert their effect by blocking the action of acetylcholine, a neurotransmitter that transmits signals within the nervous system that are responsible for the activation of sweat glands. QBREXZA is applied directly to the skin and is designed to block underarm sweat production by inhibiting sweat gland activation. We began shipping QBREXZA to wholesalers and a preferred dispensing partner (together, “Customers”) in September 2018, and QBREXZA became commercially available in pharmacies nationwide on October 1, 2018. Lebrikizumab, a novel, injectable, humanized monoclonal antibody targeting interleukin 13 (“IL-13”) that we are developing for the treatment of moderate-to-severe atopic dermatitis. IL-13 is a naturally occurring cytokine that is thought to play an important role in promoting allergic inflammation and mediating its effects on bodily tissues, including in patients with atopic dermatitis. Lebrikizumab is designed to bind to IL-13 with high affinity, specifically preventing formation of the IL-13 receptor/interleukin 4 (“IL-4”) receptor complex and subsequent signaling. In August 2017, we entered into a license agreement (the “Roche Agreement”) with F. Hoffmann-La Roche Ltd and Genentech, Inc. (together, “Roche”) pursuant to which we obtained exclusive, worldwide rights to develop and commercialize lebrikizumab for atopic dermatitis and all other therapeutic indications. Based on the results of two exploratory Phase 2 clinical trials conducted by Roche in atopic dermatitis patients, we initiated a Phase 2b clinical trial in January 2018 to evaluate the safety and efficacy of lebrikizumab as a monotherapy compared with placebo and to establish the dosing regimen for a potential Phase 3 program in patients with moderate-to-severe atopic dermatitis. We completed enrollment of 280 patients ages 18 years and older in the Phase 2b clinical trial in October 2018 and expect to announce topline results in the second half of March 2019. Early-stage research and development programs in other areas of dermatology.





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### Our Strategy

Our strategy is to develop and commercialize innovative and differentiated therapies that we believe can advance the standard of care for patients with dermatologic diseases. The key components of our strategy are to:

Commercialize QBREXZA and any other products for which we secure marketing approval. We are commercializing QBREXZA and currently plan to commercialize our other approved products, if any, in the United States by deploying a specialized sales force targeting primarily dermatologists, as well as other healthcare practitioners. We believe that we can compete effectively in the medical dermatology market by having our own sales and marketing and medical affairs organizations that provide high levels of customer support and scientific expertise to patients, dermatologists and other healthcare practitioners. We may partner with third parties to help us reach additional geographic markets or medical specialties. For example, we have granted an exclusive license to Maruho Co., Ltd. (“Maruho”) to develop and commercialize glycopyrronium tosylate for the treatment of hyperhidrosis in Japan.

Rapidly develop our lebrikizumab product candidate. In our QBREXZA program, we produced positive Phase 2b clinical trial results within nine months of initiating our first clinical trial and positive Phase 3 clinical trial results within 10 months of initiating our Phase 3 clinical program. In our lebrikizumab program, we initiated our first clinical trial within five months of the closing of the Roche Agreement and completed patient enrollment in this clinical trial within nine months thereafter. We believe that our team’s expertise in designing and executing product development programs in medical dermatology will enable us to rapidly develop our lebrikizumab product candidate.

Efficiently establish proof of concept for early stage product candidates and advance promising candidates into late stage development. In developing early stage product candidates, we focus on translating advances in the understanding of skin disease biology into innovative solutions for unmet needs in dermatology. We seek to rapidly and efficiently establish proof of concept for these product candidates. Using this approach, our experienced management team is able to efficiently determine whether and how to advance product candidates into the next stages of development, which we believe increases our ability to direct resources to promising programs and enhances our likelihood of successfully developing and commercializing our product candidates.

In license and acquire new products and product candidates. Since our founding in 2010, we have executed multiple transactions resulting in our existing portfolio. For example, in April 2013, we entered into agreements with Rose U LLC (“Rose U”) and Stiefel Laboratories, Inc., a GSK company (“Stiefel”), to obtain rights to intellectual property related to our hyperhidrosis program. In August 2017, we entered into the Roche Agreement pursuant to which we obtained exclusive, worldwide rights to develop and commercialize lebrikizumab for atopic dermatitis and all other therapeutic indications. We intend to continue to identify, evaluate, in license and acquire products and product candidates from various sources by leveraging the insights, network and experience of our management team. Our objective is to maintain a well balanced portfolio and leverage our development and commercial capabilities by in licensing or acquiring additional products and product candidates across various stages of development and commercialization.

Continue to build a team of committed, experienced employees and engage with patients and members of the dermatology community. We believe that the field of medical dermatology offers a unique opportunity to build relationships with medical practitioners, opinion leaders, patients and advocacy groups. We believe that consolidation in the medical dermatology industry has resulted in an enhanced opportunity for a medical dermatology focused company to build relationships with these stakeholders and has made available a large and growing talent pool of experienced employees who can make significant contributions to our company.

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Our Product and Product Candidates Portfolio

Our portfolio of product and product candidates is summarized in the following figure:

\*Worldwide rights subject to option and license agreement with Almirall, S.A.

QBREXZA

Overview

QBREXZA, a topical, once-daily anticholinergic cloth, was approved by the FDA in June 2018 for the treatment of primary axillary hyperhidrosis in adult and pediatric patients nine years of age and older. Primary axillary hyperhidrosis is a medical condition with no known cause that results in underarm sweating beyond what is needed for normal body temperature regulation. QBREXZA is applied directly to the skin and is designed to block underarm sweat production by inhibiting sweat gland activation. We began shipping QBREXZA to Customers in September 2018, and QBREXZA became commercially available in pharmacies nationwide on October 1, 2018.

In the body, sweat is produced by glands in the skin and released to the skin surface through ducts. Sweat gland activity is controlled by the nervous system. The nervous system transmits signals to the sweat glands through a neurotransmitter called acetylcholine. Anticholinergics are a class of pharmaceutical products that exert their effect by blocking the action of acetylcholine.

Primary hyperhidrosis can affect the underarms, palms of the hands, soles of the feet, face and other areas. According to a study published in 2016, the prevalence of hyperhidrosis in the United States is estimated to be 4.8% of the population, or approximately 15.3 million people. According to this study, 65% of hyperhidrosis sufferers in the United States have axillary hyperhidrosis. Additionally, several studies have demonstrated that excessive sweating often impedes normal daily activities and can result in occupational, emotional, psychological, social and physical impairment. Studies also suggest that the negative impact caused by excessive sweating has been reported to be similar to, if not greater than, the negative impact caused by conditions such as psoriasis and other chronic diseases. There are very few approved treatments for hyperhidrosis, and the unmet medical need remains high.

The market for products to control sweating is large and highly underpenetrated by prescription pharmaceutical products. Despite the limited efficacy of over the counter (“OTC”) antiperspirants for the alleviation of hyperhidrosis symptoms, according to the 2016 study, only about half of patients suffering from hyperhidrosis have discussed their condition with a healthcare professional (“HCP”). The reasons most commonly cited by hyperhidrosis sufferers for not discussing their excessive sweating with an HCP are lack of awareness that hyperhidrosis is a medical condition and belief that nothing can be done to treat their condition. Of those who do see an HCP about their excessive sweating, 53% were diagnosed with hyperhidrosis. In addition, patients may suffer from excessive sweating for years before seeking treatment. One study analyzing data from 1993–2005 indicated that patients experienced an average duration of untreated symptoms of 8.9 years. We believe that this is largely a

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result of the lack of effective, well tolerated and convenient prescription treatment options. For example, according to a survey of 398 axillary hyperhidrosis sufferers in the United States conducted by Dermira in July 2018 prior to the launch of QBREXZA, approximately two-thirds of those surveyed indicated they were not satisfied with the products they were currently using to treat their condition. Patients who seek treatment from a physician most commonly receive prescription topical antiperspirants. According to data provided by IQVIA NPA, these topical antiperspirants generated approximately 408,000 prescriptions in the United States in 2018. However, their use is limited by modest efficacy, particularly in patients with more severe disease and skin irritation. We believe that the market opportunity for a new, effective, well tolerated and self-administered prescription topical axillary hyperhidrosis treatment is substantially larger than the current market for prescription topical antiperspirants because such a therapy could further penetrate the segment of patients who seek treatment from a physician and encourage more patients to seek treatment. Prior to the availability of QBREXZA, therapeutic options for patients who are unsatisfied with topical antiperspirants are largely limited to more cumbersome or invasive strategies directed to blocking the activation of, destroying or removing the sweat glands by injectable, systemic, surgical or other means. These treatment options, which include injectable botulinum toxin (“Botox”) and off label use of oral anticholinergic agents, are often poorly tolerated and are used much less frequently than topical therapies. QBREXZA is the first and only FDA-approved once-daily, topical prescription treatment for the treatment of primary axillary hyperhidrosis.

### Clinical Development

Prior to FDA approval of QBREXZA, three Phase 2 clinical trials and three Phase 3 clinical trials to evaluate efficacy and safety were completed. The Phase 3 program comprised two pivotal clinical trials named ATMOS-1 and ATMOS-2 that were designed to assess the safety and efficacy of QBREXZA relative to vehicle and one clinical trial named ARIDO that was designed to assess the long-term safety of QBREXZA.

The ATMOS-1 and ATMOS-2 Phase 3 trials were conducted in subjects with primary axillary hyperhidrosis and enrolled a total of 697 patients nine years of age or older. Inclusion criteria required that prior to the start of treatment, all subjects produce at least 50 mg of sweat in each axilla over a 5-minute period and rate the severity of their sweating daily over a week with a mean score of 4 or higher on the Axillary Sweating Daily Diary (“ASDD”) item #2, a patient reported outcome instrument scored from 0 (no sweating) to 10 (worst possible sweating). The median sweat production over 5 minutes at baseline was 122 mg in the QBREXZA arm and 113 mg in the vehicle arm in Trial 1, and 127 mg in the QBREXZA arm and 117 mg in the vehicle arm in Trial 2. The average weekly mean score on the ASDD item #2 at baseline was approximately 7.2 across both trials.

Subjects were randomized to receive either QBREXZA or vehicle applied once daily to each axilla. The co-primary endpoints were the proportion of subjects having at least a 4-point improvement from baseline in the weekly mean ASDD item #2 score at week 4 and the mean absolute change from baseline in gravimetrically measured sweat production at week 4.

The results of ATMOS-1 (“Trial 1”) and ATMOS-2 (“Trial 2”) are presented in the table below:

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### Lebrikizumab

#### Overview

Lebrikizumab is our late-stage product candidate for the treatment of moderate-to-severe atopic dermatitis. IL-13 is a naturally occurring molecule that is thought to play a central role in promoting allergic inflammation and mediating its effects on bodily tissues, including in patients with atopic dermatitis. Lebrikizumab is designed to bind IL-13 with high affinity, specifically preventing formation of the IL-13 receptor/IL-4 receptor complex and subsequent signaling, thereby inhibiting the biological effects of IL-13 in a targeted and efficient fashion. Roche has studied lebrikizumab in clinical trials involving more than 4,000 subjects across a range of conditions, such as asthma, chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis, including two exploratory Phase 2 clinical trials in moderate-to-severe atopic dermatitis patients. In August 2017, we entered into a licensing agreement with Roche pursuant to which we obtained exclusive, worldwide rights to develop and commercialize lebrikizumab for atopic dermatitis and all other therapeutic indications.

Atopic dermatitis is the most common and severe form of eczema, a chronic inflammatory condition that can present as early as childhood and continue into adulthood. It is estimated to affect 12% of children and 10% of adults. A complex disorder involving an interplay of immune system dysfunction, skin barrier compromise and environmental exposures, atopic dermatitis is characterized by dry, itchy, red, swollen and/or cracked skin, often accompanied by increased risk of infection, as well as intense, persistent itching that exacerbates skin barrier disruption and other clinical symptoms. Moderate-to-severe disease can cover much of the body and have a profound, negative impact on patients' mental and physical functioning, limiting their sleep quality, activities and health-related quality of life.

Atopic dermatitis is commonly treated with topical products, including moisturizing emollients, corticosteroids and calcineurin inhibitors, as well as topical and oral antimicrobial therapies to manage skin infections and antihistamines to aid in the management of itch. Moderate-to-severe disease is often treated with systemic, immunomodulatory therapy, most commonly oral corticosteroids and less frequently other immunosuppressants, such as methotrexate, cyclosporine, azathioprine and mycophenolate mofetil, which carry risks of well-documented side effects, including kidney, liver and blood toxicity, that require intensive monitoring by the prescribing physician during long-term use. In March 2017, Dupixent, a monoclonal antibody that inhibits IL-4 and IL-13 signaling by binding to the IL-4 receptor subunit, became the first systemic therapy specifically approved by the FDA for the treatment of atopic dermatitis, offering a significant advance in treatment based on its efficacy and lack of systemic side effects associated with oral corticosteroids and other immunosuppressants.

The introduction of new, targeted therapies, such as Dupixent, is projected to transform the treatment of moderate-to-severe atopic dermatitis in much the same way that the advent of biologic therapies transformed the treatment of moderate-to-severe psoriasis over the past 15 years. Prior to FDA approval of the first biologic therapy for psoriasis in 2003, moderate-to-severe psoriasis was treated with many of the same oral immunosuppressants used to treat atopic dermatitis today, with moderate efficacy and well-documented side effects. According to Decision Resources, since the FDA approved the first biologic therapy for psoriasis in 2003, and with the subsequent introduction of systemic, biologic and small-molecule therapies targeting a range of inflammatory mediators, the market for psoriasis therapies in the United States has grown approximately tenfold and is projected to total more than \$13 billion in sales in 2025.

In comparison with psoriasis, which Decision Resources estimates currently affects approximately 8.6 million people in the United States, of whom approximately 1.7 million suffer from moderate-to-severe disease, atopic dermatitis is estimated to affect 33 million people in the United States, of whom approximately 7 million suffer from moderate-to-severe disease. With the introduction of new, targeted therapies, such as Dupixent, Decision Resources estimates that sales of atopic dermatitis medications in the United States will grow from approximately \$0.8 billion in

2016 to approximately \$14.8 billion by 2025.

IL-13 and Lebrikizumab. IL-13 is thought to play a central role in promoting allergic inflammation and mediating its effects on bodily tissues in atopic dermatitis and other allergic diseases. Studies suggest that IL-13 contributes to many of the characteristic manifestations of atopic dermatitis, including skin barrier dysfunction, itch, infection and skin remodeling. In promoting allergic inflammation, IL-13 stimulates recruitment, activation and maturation of immune cells, including production of inflammatory mediators. In the skin, IL-13 is highly expressed

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in atopic dermatitis lesions, where expression levels appear to correlate with lesion severity and chronicity. IL-13 mediates the effects of inflammation on skin tissue via several means. It is hypothesized that dysregulation of IL-13 disrupts the skin's ability to serve as an effective barrier to environmental exposures, and it has been established that IL-13 down-regulates production of structural proteins that are important for maintenance of skin barrier integrity. In addition to its impact on skin barrier function, recent research has shown that IL-13 is a neuronal enhancer in multiple itch pathways and may be driving chronic itch in atopic dermatitis. IL-13 also suppresses immune responses to infectious microbes and stimulates collagen production and skin remodeling, suggesting it may contribute to the increased rate of infection and dysregulated skin tissue repair observed in atopic dermatitis patients. Blocking IL-13 has been shown to increase production of skin barrier proteins, reduce sensitivity to mediators of itch, enhance responses to infectious microbes, reduce tissue remodeling and reduce inflammation in preclinical models of atopic dermatitis. Successful treatment of atopic dermatitis normalizes both IL-13 expression and IL-13 mediated signaling. Recent clinical studies have demonstrated improvements in signs and symptoms in atopic dermatitis patients treated with monoclonal antibodies targeting IL-13.

We believe that lebrikizumab may offer an attractive and differentiated approach to the treatment of atopic dermatitis. Based on the central role of IL-13 in atopic dermatitis and lebrikizumab's unique molecular profile, combining a differentiated mechanism of action, high affinity for its target and robust pharmacokinetics, we believe targeting IL-13 with lebrikizumab presents an opportunity to deliver a therapy with a compelling combination of safety, tolerability, efficacy, convenience and ease of use to people living with moderate-to-severe atopic dermatitis and the HCPs who care for them. Lebrikizumab is designed to bind IL-13 with high affinity, specifically preventing formation of the IL-13 receptor/IL-4 receptor complex and subsequent signaling, thereby inhibiting the biological effects of IL-13 in a targeted and efficient fashion. From a pharmacokinetic standpoint, whereas many antibodies that bind receptor proteins are rapidly cleared from the body following binding to their targets, lebrikizumab, like many antibodies that bind circulating proteins, such as IL-13, is cleared from the body more slowly, suggesting it could potentially be administered less frequently than other antibodies. Relative to other antibodies targeting IL-13, lebrikizumab has high affinity for its target, as well as a differentiated mechanism of action that does not involve inhibition of the binding of IL-13 to an alternate IL-13 receptor that serves as a natural regulator of IL-13 activity. Relative to small molecules, such as those that inhibit widespread cellular signaling proteins called janus kinases ("JAK inhibitors"), thereby broadly reducing the transmission of immune responses induced by a range of stimuli, evidence suggests targeted inhibition of IL-13 via monoclonal antibodies like lebrikizumab could result in a lower risk of side effects and associated clinical monitoring requirements, in addition to requiring substantially less frequent administration. As a result, we believe that lebrikizumab could be safer, better tolerated, more effective, more convenient and/or easier to use than Dupixent and many other products in development for atopic dermatitis.

Roche studied lebrikizumab in clinical trials involving more than 4,000 subjects across a range of conditions, including two exploratory Phase 2 clinical trials in moderate-to-severe atopic dermatitis patients. In addition to the initial efficacy results generated in atopic dermatitis patients, we believe the substantial safety experience accumulated across the lebrikizumab program to date is supportive of the development of lebrikizumab in atopic dermatitis.

Additionally, the potentially important role of IL-13 in mediating the effects of inflammation across multiple bodily tissues suggests that lebrikizumab may have applicability in conditions beyond atopic dermatitis. We intend to consider further investigating diseases in which inhibition of IL-13 can have potential therapeutic benefits for patients.

### Clinical Development in Atopic Dermatitis

**Phase 2a Clinical Trials.** In addition to a number of studies in other potential indications, Roche has completed two exploratory Phase 2 clinical trials evaluating lebrikizumab in adults with moderate-to-severe atopic dermatitis.

TREBLE Phase 2 Exploratory Clinical Study. The TREBLE study was a randomized, placebo-controlled, double-blind, Phase 2, proof-of-concept study designed and conducted by Roche to assess the efficacy and safety of lebrikizumab, administered via subcutaneous injection as add-on therapy to twice-daily topical corticosteroids (“TCS”) in 209 adult patients with moderate-to-severe atopic dermatitis. Dosing in this study was largely based on

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experience with lebrikizumab in asthma clinical trials and the objective of characterizing both dose-response relationships and dosing frequency requirements in atopic dermatitis.

After two weeks of twice daily TCS therapy, patients in the TREBLE study were randomized 1:1:1:1 to receive either a single dose of 125 milligrams (“mg”) of lebrikizumab plus continued TCS (n=52), a single, 250-mg dose of lebrikizumab plus TCS (n=53), 125 mg of lebrikizumab every four weeks (“q4w”) plus TCS (n=51), or placebo q4w plus TCS (n=53), for up to 12 weeks. The primary endpoint was the percentage of patients achieving a 50% reduction from baseline in the 72-point clinical grading scale called the Eczema Area and Severity Index (“EASI-50”), an endpoint that has been widely used to measure treatment success in clinical atopic dermatitis trials, at the end of the 12-week treatment period. In addition, the time course of response to lebrikizumab treatment was assessed via a range of other measures, including EASI-50, as well as the proportion of patients achieving a 75% reduction from baseline in EASI score (“EASI-75”), the proportion of patients achieving a 90% reduction from baseline in EASI score (“EASI-90”), and the proportion of patients achieving clearing or near clearing of atopic dermatitis, as rated by the investigator on a five-point scale called the Investigator Global Assessment that ranges from zero, representing clear skin, to four, representing severe disease (“IGA0/1”). Inclusion criteria required that patients had an inadequate response to TCS and a regular emollient, and at both screening and the end of the initial two weeks of TCS treatment prior to the initiation of lebrikizumab treatment, had an EASI score of at least 14 and an IGA score of at least three.

The results of the TREBLE study provided proof-of-concept for the treatment of atopic dermatitis with lebrikizumab, including information we believe that we can use to optimize the clinical profile of lebrikizumab in future clinical trials. Across a number of key efficacy measures employed in this study, lebrikizumab provided clinically meaningful placebo-corrected improvements, generally in a dose-dependent manner. These improvements were observed on top of intensive TCS application that was associated with substantial responses in the placebo group.

#### Efficacy across Key Measures over 12 Weeks

P-values shown above are as of the end of the 12-week treatment period and represent comparisons to corresponding data in patients who received placebo only. P-values of less than 0.05 are denoted by \*.

After 12 weeks of treatment, relative to patients who received placebo, the group of patients who received 125 mg of lebrikizumab q4w achieved statistically significant improvements in the primary endpoint, EASI-50 (82.4% vs. 62.3%, p=0.03). Improvements were also seen in the EASI-75 (54.9% vs. 34.0%, p=0.04) and EASI-90 (25.5% vs. 9.4%, p=0.03). The percentage of subjects achieving IGA0/1 was 33.3% in the 125 mg lebrikizumab group and 18.9% in the placebo group (p=0.10). In these patients, placebo-adjusted efficacy across these measures did not appear to plateau at the end of the 12-week treatment period, consistent with the fact that in the absence of a loading dose, circulating lebrikizumab concentrations likely did not reach a steady state during this period. While the groups of patients who received single, 125- or 250-mg doses of lebrikizumab generally did not achieve statistically significant improvements relative to those who received placebo after 12 weeks of observation in this study, results in these patients showed that placebo-adjusted effects on disease severity appeared to peak several weeks following the administration of a single lebrikizumab injection.



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We believe that the dose-response relationships observed across multiple endpoints, as well as trends toward improved efficacy with increasing dose and duration, suggest that increasing the dose and/or duration of repeated administration of lebrikizumab may result in improved efficacy in ongoing and future clinical atopic dermatitis trials, an effect that may be further improved by the introduction of a loading dose to achieve steady-state circulating lebrikizumab concentrations shortly after the start of therapy. Additionally, we believe that the time course of the responses observed in the TREBLE study, including following single doses of lebrikizumab, suggest that it may be feasible to administer lebrikizumab q4w, if not less frequently, in atopic dermatitis.

**ARBAN Phase 2 Exploratory Clinical Study.** ARBAN was an open-label study designed to assess the safety of lebrikizumab as a monotherapy, with an exploratory assessment of efficacy, in adult patients with moderate-to-severe atopic dermatitis. Clinical improvements were observed in patients treated with lebrikizumab.

**Safety and Tolerability.** Consistent with results observed across the lebrikizumab program to date, lebrikizumab was generally well-tolerated in these exploratory clinical studies in atopic dermatitis. There were no imbalances in the proportions of patients reporting adverse events, serious adverse events, events leading to discontinuation, or overall infections when comparing all lebrikizumab-treated patients with controls. Four patients (2.2%) in the lebrikizumab groups (all doses combined) and two control patients (2.5%) experienced an adverse event that led to withdrawal from the studies. Injection-site reactions occurred infrequently (in 1.2% of patients in all lebrikizumab groups and 1.3% of control patients).

**Phase 2b Clinical Program.** In January 2018, we initiated a randomized, double-blind, placebo-controlled, parallel-group, Phase 2b dose-ranging study to evaluate the safety and efficacy of lebrikizumab as a monotherapy in patients with moderate-to-severe atopic dermatitis. Based on early clinical experience with lebrikizumab, the study is designed to build on the body of evidence supporting targeting of IL-13 in atopic dermatitis by evaluating three different dosing regimens, with the objective of optimizing the clinical profile of lebrikizumab and establishing the dosing regimen for a potential Phase 3 program. The study enrolled 280 patients ages 18 years and older with moderate-to-severe atopic dermatitis in the United States randomized in a 3:3:3:2 fashion as follows:

- ◆ Group 1: A loading dose of 250 mg of lebrikizumab at week zero, followed by 125 mg of lebrikizumab every four weeks.
- ◆ Group 2: A loading dose of 500 mg of lebrikizumab at week zero, followed by 250 mg of lebrikizumab every four weeks.
- ◆ Group 3: A loading dose of 500 mg of lebrikizumab at weeks zero and two, followed by 250 mg of lebrikizumab every two weeks.
- ◆ Group 4: Placebo at week zero and every two weeks thereafter.

The primary endpoint of the study is the percent change in the EASI score from baseline to week 16. Key secondary endpoints that will be evaluated during the 16-week treatment period include EASI-50, EASI-75 and EASI-90; the proportion of patients with an IGA score of zero (clear) or one (almost clear) and a reduction of two or more points (on a five-point scale) from baseline; and changes in pruritus (itch) and sleep loss and scores from baseline, both scored using 11-point numerical rating scales. Key inclusion criteria for patients enrolled in this study include chronic atopic dermatitis for at least one year, an EASI score of 16 or greater, an IGA score of three or four, and involvement of at least 10% of body surface area at screening and baseline. Following the end of the 16-week treatment period, patients will be followed for an additional 16 weeks.

This Phase 2b clinical trial completed enrollment in October 2018 and we expect topline results in the second half of March 2019.

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### Research and Development Programs

We continue to work on other compounds in early stages of development. In August 2016, we entered into an exclusive option and license agreement with Takeda Pharmaceutical Company Limited (“Takeda”) pursuant to which we acquired an option to license exclusive worldwide rights for three early-stage programs with undisclosed mechanisms of action as potential topical treatment options for dermatologic diseases. In December 2017, we acquired from Takeda an option to license exclusive worldwide rights for an additional early-stage program. If we exercise our option for any program, we would obtain an exclusive, worldwide license to develop and commercialize selected compounds from that program and be solely responsible for further research, development and commercialization costs related to these compounds. In December 2018, we exercised our option with respect to one of the early-stage programs and obtained an exclusive, worldwide license to develop and commercialize selected compounds from that program as potential topical treatment options for dermatologic diseases.

### Competition

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

Many of our competitors 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 if our competitors develop or market products or other novel therapies that are more effective, safer or less costly than our current or future product candidates, or obtain regulatory approval for their products more rapidly than we may obtain approval for our product candidates. Our success will be based in part on our ability to identify, develop and manage a portfolio of product candidates that are differentiated in relation to competing products.

### Primary Axillary Hyperhidrosis

QBREXZA competes with other therapies used for primary axillary hyperhidrosis, including:

- **Self Administered Treatments.** Self administered treatments include OTC and prescription topical antiperspirants. Oral and compounded topical anticholinergics may also be used off label.
- **Non Surgical Office Based Procedures.** Office based procedures have been approved for the treatment of primary axillary hyperhidrosis, including Botox intradermal injections marketed by Allergan plc (“Allergan”), and device-based treatments, such as MiraDry, a microwave treatment marketed by Miramar Labs, Inc., a subsidiary of Sientra, Inc., and PrecisionTx, a laser procedure from Cynosure, Inc.
  - **Surgical Treatments.** Surgical treatments include techniques for the removal of sweat glands, such as excision, curettage and liposuction. Surgical procedures, such as endoscopic thoracic sympathectomy, also are used to destroy nerves that transmit activating signals to sweat glands.

In addition, there are several treatments under development that could potentially be approved and used to treat primary axillary hyperhidrosis and compete with QBREXZA, including: energy-based devices from Candasant Biomedical, Inc., and Ulthera, Inc., a subsidiary of Merz Pharma GmbH & Co. KGaA; topical forms of botulinum toxin from Allergan and Eirion Therapeutics, Inc.; an injectable form of botulinum toxin from Medytox Inc.; topical anticholinergic product candidates from Brickell Biotech, Inc., Dr. August Wolff GmbH & Co. and GlaxoSmithKline LLC (“GSK”); and oral anticholinergic product candidates from Dermavant Sciences, Inc., a division of Roivant Sciences Ltd., and Atacama Therapeutics, Inc.



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### Atopic Dermatitis

If approved for the treatment of moderate-to-severe atopic dermatitis, we anticipate that lebrikizumab would compete with other approved and marketed prescription atopic dermatitis products, including:

**Injected Biologic Products.** Dupixent, a monoclonal antibody targeting IL-4 and IL-13 signaling marketed by Regeneron Pharmaceuticals, Inc. (“Regeneron”) and Sanofi-Aventis Groupe S.A. (“Sanofi”), is the only systemic therapy currently approved by the FDA specifically to treat atopic dermatitis. Monoclonal antibodies targeting other molecules, such as Xolair, a monoclonal antibody targeting immunoglobulin E marketed by Roche and Novartis AG (“Novartis”), may be used off-label.

**Other Systemic Treatments.** Other systemic treatments are prescribed for the treatment of moderate-to-severe atopic dermatitis, including branded and generic oral corticosteroids, generic injectable and oral methotrexate products marketed by Sandoz International GmbH, a division of Novartis (“Sandoz”), Mylan N.V. (“Mylan”), Teva Pharmaceutical Industries Ltd. (“Teva”) and Hospira, Inc., a subsidiary of Pfizer Inc. (“Pfizer”); branded oral cyclosporine products such as Neoral, marketed by Novartis, and Gengraf, marketed by AbbVie Inc. (“AbbVie”); generic oral cyclosporine products marketed by Sandoz and IVAX Corporation, a subsidiary of Teva; branded oral mycophenolate products, such as CellCept, marketed by Roche, and Myfortic, marketed by Novartis; and generic oral mycophenolate products marketed by Mylan, Sandoz and Teva.

**Other Therapies.** Oral antibiotics and antihistamines are often used to manage comorbidities of atopic dermatitis, such as skin infections, and symptoms of atopic dermatitis, such as itch, respectively. There are also several prescriptions, non-prescription and OTC topical products utilized to treat atopic dermatitis, including Eucrisa, marketed by Pfizer, topical corticosteroids and topical calcineurin inhibitors, as well as bath solutions and moisturizers.

In addition to moderate-to-severe atopic dermatitis treatments that are currently available for commercial use, there are several pharmaceutical product candidates that are under development and could potentially be used to treat atopic dermatitis and compete with lebrikizumab. Product candidates in Phase 3 development include tralokinumab from LEO Pharma A/S (“LEO Pharma”), baricitinib from Eli Lilly and Company (“Eli Lilly”), PF 04945842 from Pfizer and upadacitinib from AbbVie. There are also product candidates in earlier stages of development that could potentially be used to treat atopic dermatitis and compete with lebrikizumab, including products currently being developed by AbbVie; Asana Biosciences, LLC; AnaptysBio, Inc.; Amgen Inc. (“Amgen”) and MedImmune, LLC, a division of AstraZeneca PLC; ASLAN Pharmaceuticals; Chugai Pharmaceutical Co., a division of Roche, Galderma S.A., a division of Nestle Skin Health S.A., and Maruho; Suzhou Connect Biopharmaceuticals, Ltd., DS BioPharma Limited; Eli Lilly; Galapagos NV, MorphoSys AG and Novartis; GSK; Glenmark Pharmaceuticals Limited; Kiniksa Pharmaceuticals, Ltd.; Kymab Limited; Kyowa Hakko Kirin Co., Ltd.; LEO Pharma; Menlo Therapeutics Inc.; Novartis; Pfizer; Regeneron and Sanofi; Roche; Vanda Pharmaceuticals Inc., and XBiotech Inc.

### Commercial Operations

We have built a commercial infrastructure to support the commercialization of QBREXZA and the potential commercialization of additional products in the United States. We have built a sales force of over 100 sales representatives to establish relationships with dermatologists, as well as other healthcare practitioners and other prescribers. Our sales force is supported by our commercial group, including sales management, an internal marketing group, market access and payer efforts, and professional relations, as well as our separate medical affairs and supply chain management groups. In addition to our efforts with physicians, we are committing and will continue to commit financial and management resources to engage patients directly. To support our commercial infrastructure, we plan to continue to invest significant financial and management resources. We may also partner with third parties to help us reach other geographic markets or therapeutic specialties.

For 2018, sales of QBREXA accounted for \$3.0 million or 7.0% of our revenues, while in 2017 and 2016, all of our revenues were from collaboration and license agreements.

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### Intellectual Property

Our success depends in large part upon our ability to obtain and maintain proprietary protection for our products and technologies, and to operate without infringing the proprietary rights of others. With respect to the former, our policy is to protect our proprietary position by, among other methods, filing patent applications on inventions that are important to the development and conduct of our business with the U.S. Patent and Trademark Office (“USPTO”) and its foreign counterparts. We seek to avoid the latter by monitoring patents and publications that may affect our business, and to the extent we identify such developments, evaluate and take appropriate courses of action.

As of December 31, 2018, we own or have an exclusive license to 35 issued U.S. patents and 132 issued foreign patents, which include granted European patent rights that have been validated in various EU member states, and 10 pending U.S. patent applications and 79 pending foreign patent applications.

Issued U.S. and foreign patents and pending U.S. and foreign patent applications, if issued, for our lead product candidates, glycopyrronium tosylate and lebrizumab, will expire between 2020 and 2037.

We also use other forms of protection, such as trademark, copyright and trade secret protection, to protect our intellectual property, particularly where we do not believe patent protection is appropriate or obtainable. We aim to take advantage of all of the intellectual property rights that are available to us and believe that this comprehensive approach will provide us with proprietary positions for our product candidates, where available.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country.

We also protect our proprietary information by requiring our employees, consultants, contractors and other advisors to execute nondisclosure and assignment of invention agreements upon commencement of their respective employment or engagement. Agreements with our employees also prevent them from bringing the proprietary rights of third parties to us. In addition, we also require confidentiality or service agreements from third parties that receive our confidential information or materials.

### Collaboration and License Agreements

#### Agreements with Rose U and Stiefel

In April 2013, we entered into an exclusive license agreement with Rose U pursuant to which we obtained a worldwide exclusive license within a field of use including hyperhidrosis to practice, enforce and otherwise exploit certain patent rights, know how and data related to our hyperhidrosis program. The license agreement with Rose U included a sublicense of certain data and an assignment of certain regulatory filings which Rose U had obtained from Stiefel. In connection with the license agreement, we entered into a letter agreement with Stiefel pursuant to which we assumed Rose U’s obligation to pay Stiefel approximately \$2.5 million in connection with the commercialization of products developed using the licensed data and to indemnify Stiefel for claims arising from the use, development or commercialization of products developed using the Stiefel data. The agreements require us to use commercially reasonable efforts to develop and commercialize products using the licensed patent rights, know how and data.

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As of December 31, 2018, we have paid license and other fees of \$4.3 million to Rose U and Stiefel, including a \$2.5 million payment in connection with the first commercial sale of QBREXZA, and are required to pay Rose U additional amounts totaling up to \$0.6 million upon the achievement of certain regulatory milestones and other contingent payments. In addition, we are obligated to pay Rose U low-to-mid single-digit royalties on net product sales and low double-digit royalties on sublicense fees and certain milestone, royalty and other contingent payments received from sublicensees, to the extent such amounts are in excess of the milestone and royalty payments we are obligated to pay Rose U or its assignee directly upon the events or sales triggering such payments. We are entitled to credit the \$2.5 million milestone payment against current and future royalty payments owed to Rose U in accordance with the terms of the license agreement.

We are permitted to grant sublicenses to the licensed rights and may assign the agreements upon an acquisition of us or our assets that relate to the license agreement, provided that in the event of an acquisition of our assets we must first pay to Stiefel the commercialization payment we are obligated to make on behalf of Rose U, if such amount has not already been paid. We may terminate the license agreement if Rose U experiences certain insolvency events or if Rose U commits a material breach of the license agreement, subject to applicable cure provisions. We may also terminate the license agreement if we determine that development results or market dynamics do not justify further development or commercialization of licensed products, in which case, all patent and technology rights shall revert to Rose U and we will (1) grant Rose U a perpetual nonexclusive license to any improvements owned by us related to the Rose U intellectual property that have been applied to or used with our hyperhidrosis program, at a royalty rate to be mutually agreed through good faith negotiation, and (2) for 120 days after such termination, assist and cooperate with Rose U (at Rose U's expense) in connection with the license of such improvements to Rose U. Rose U may terminate the license in certain circumstances if we experience certain insolvency events or if we commit a material breach of the license agreement or if we cause Rose U to be in material breach of its license agreement with Stiefel, subject in each case to applicable cure provisions. Subject to earlier termination, the license agreement remains in effect until 15 years following the first commercial sale of a licensed product have elapsed or, if later, the date that the last patent or patent application in the licensed patent rights has expired or been revoked, invalidated or abandoned. The last to expire issued patent that we licensed under the license agreement with Rose U expires in 2029.

### Agreements with Maruho

In March 2013, we entered into a Right of First Negotiation Agreement with Maruho ("Maruho Right of First Negotiation Agreement"), pursuant to which we provided Maruho with certain information and the right to negotiate an exclusive license to develop and commercialize certain of our products in specified territories. In connection with the entry into this agreement, Maruho paid us \$10.0 million ("Maruho Payment"), which will be credited against certain payments payable by Maruho to us if we enter into a license agreement for any of our products with Maruho. Maruho's right of first negotiation expired in December 2016 but the right to credit the Maruho Payment against certain payments under any future license agreement for our products remains.

In September 2016, we entered into an Exclusive License Agreement with Maruho, which grants Maruho an exclusive license to develop and commercialize glycopyrronium tosylate for the treatment of hyperhidrosis in Japan ("Maruho G.T. Agreement"). Pursuant to the terms of the Maruho G.T. Agreement, we received an upfront payment of \$25.0 million from Maruho in October 2016 and are eligible to receive additional payments totaling up to \$70.0 million, contingent upon the achievement of certain milestones associated with submission and approval of a marketing application in Japan and certain sales thresholds, as well as royalty payments based on a percentage of net product sales in Japan. The Maruho G.T. Agreement further provides that Maruho will be responsible for funding all development and commercial costs for the program in Japan and, until such time, if any, as Maruho elects to establish its own source of supply of drug product, Maruho will purchase product supply from us for development and, if applicable, commercial purposes at cost. The Maruho G.T. Agreement is unrelated to, and the exclusive license of glycopyrronium tosylate in Japan to Maruho was not subject to the terms of, the Maruho Right of First Negotiation

Agreement.

Unless earlier terminated, the Maruho G.T. Agreement will remain in effect until the later of: (1) expiration or abandonment of the last valid claim of the applicable patent rights in Japan; (2) expiration of any market exclusivity in Japan granted by the applicable regulatory authority; and (3) 15 years following the date of the first commercial sale of the drug product in Japan.

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### Agreement with Roche

In August 2017, we entered into the Roche Agreement pursuant to which we obtained exclusive, worldwide rights to develop and commercialize lebrikizumab, an injectable, humanized antibody targeting IL 13, for atopic dermatitis and all other therapeutic indications. Unless earlier terminated, the Roche Agreement will remain in effect until no royalty or other payment obligations are or may become due.

Under the terms of the Roche Agreement, we made an initial payment of \$80.0 million to Roche in October 2017 and additional payments to Roche in 2018 totaling \$55.0 million. We will also be obligated to make payments upon the achievement of certain milestones, comprising \$40.0 million upon the initiation of the first Phase 3 clinical study, up to \$210.0 million upon the achievement of regulatory and first commercial sale milestones in certain territories and up to \$1.0 billion based on the achievement of certain thresholds for net sales of lebrikizumab for indications other than interstitial lung diseases. Upon regulatory approval, if obtained, we will make royalty payments representing percentages of net sales that range from the high single-digits to the high teens. Royalty payments will be made from the first commercial sale date in a country in such country and end on the later of the date that is (a) ten years after the date of the first commercial sale of lebrikizumab in such country, (b) the expiration of the last to expire valid claim of the applicable licensed compound patent rights, Dermira patent rights or joint patent rights in such country covering the use, manufacturing, import, offering for sale, or sale of lebrikizumab in such country, (c) the expiration of the last to expire valid claim of the applicable licensed non-compound patent rights in such country covering the use, import, offering for sale, or sale of the product in such country, or (d) the expiration of the last to expire regulatory exclusivity conferred by the applicable regulatory authority in such country for lebrikizumab.

### Collaboration with UCB

In March 2014, we and UCB Pharma S.A. (“UCB”), entered into a Development and Commercialisation Agreement, dated March 21, 2014 (“UCB Agreement”), which provided that we would (a) develop Cimzia (certolizumab pegol) for the treatment of psoriasis in order for UCB to seek regulatory approval from the FDA, the European Medicines Agency and the Canadian federal department for health, and (b) upon the grant of regulatory approval in the United States and Canada, promote sales of Cimzia to dermatologists and conduct related medical affairs activities in the United States and Canada.

The UCB Agreement also provided either party with the right to terminate the agreement under certain terms. We expressed our intent to terminate the UCB Agreement in accordance with its terms. As a result, we and UCB entered into an agreement on November 6, 2017, which, among other things, (a) terminated the UCB Agreement on February 15, 2018, (b) provided for the repurchase by UCB of all product rights, licenses and intellectual property relating to Cimzia, (c) specified the responsibilities and obligations of us and UCB in connection with the transition of certain activities under the UCB Agreement from us to UCB as a result of the termination of the UCB Agreement, (d) terminated UCB’s right to designate a director nominee to our board of directors and (e) provided for the resignation of UCB’s designee from our board of directors.

### Government Regulation

#### FDA Drug Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act (“FDC Act”) and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post approval monitoring and reporting, sampling and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial

sanctions, such as FDA refusal to approve a pending NDA, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution. As a result of these regulations, pharmaceutical product development and approval are very expensive and time consuming.

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Pharmaceutical product development for a new product or certain changes to an approved product in the United States typically involves preclinical laboratory and animal tests, the submission to the FDA of an IND, which must become effective before clinical testing may commence, and adequate and well controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Clinical trials to support NDAs and Biologic License Applications (“BLA”) for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess pharmacological actions, side effects associated with increasing doses and, if possible, early evidence on effectiveness. For dermatology products, Phase 2 usually involves trials in a limited patient population to determine metabolism, pharmacokinetics, the effectiveness of the drug for a particular indication, dosage tolerance and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 clinical trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites. This permits the FDA to evaluate the overall benefit risk relationship of the drug and to provide adequate information for the labeling of the drug, should it ultimately be approved for marketing. In most cases the FDA requires two adequate and well controlled Phase 3 clinical trials with statistically significant results to demonstrate the efficacy of the drug. A single Phase 3 clinical trial with other confirmatory evidence may be sufficient in rare instances where the study is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of an effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

After completion of the required activities, including clinical testing, an NDA or BLA is prepared and submitted to the FDA. FDA approval of the NDA or BLA is required before marketing of the product may begin in the United States.

The FDA also may refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an advisory committee. Advisory committee panels typically include clinicians and other experts to provide a recommendation as to whether the safety and efficacy of the product warrant approval for the proposed indication and patient population. The FDA is not bound by the recommendation of an advisory committee. Before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with the FDA’s good clinical practice requirements. Additionally, the FDA typically inspects the facility or the facilities at which the drug is manufactured, and may inspect the sponsor company and investigator sites that participated in the clinical trials. The FDA will not approve the product unless compliance with current good manufacturing practice (“cGMP”) is satisfactory and the NDA or BLA contains data that provide substantial evidence that the drug is safe and effective for the stated indication.

After the FDA evaluates the NDA or BLA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA’s satisfaction following FDA review of a resubmission of the NDA or BLA, the FDA will issue an approval letter.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA or BLA approval, the FDA may require a risk evaluation and mitigation strategy (“REMS”) to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals and elements to assure safe use (“ETASU”). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under

certain circumstances, special monitoring and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

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Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or BLA, or applicable supplement before the change can be implemented. An NDA or BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA generally uses the same procedures and actions in reviewing NDA or BLA supplements as it does in reviewing NDAs or BLAs.

### Section 505(b)(2) New Drug Applications

Most drug products obtain FDA marketing approval pursuant to an NDA filed under section 505(b)(1) of the FDC Act. An alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA (“505(b)(2) NDA”), which enables the applicant to rely, in part, on the FDA’s previous approval of a similar product, or published literature, in support of its application.

505(b)(2) NDAs often provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference. If the 505(b)(2) NDA applicant can establish that reliance on the FDA’s previous approval is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all, or some, of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) NDA applicant.

### Biologics

Biological products used for the prevention, treatment or cure of a disease or condition of a human being are subject to regulation under the FDC Act, except the section of the FDC Act which governs the approval of NDAs. Biological products are approved for marketing under provisions of the Public Health Service Act, via a BLA. However, the application process and requirements for approval of BLAs and BLA supplements, including review timelines, are very similar to those for NDAs and NDA supplements, and biologics are associated with similar approval risks as other drugs.

### Post Approval Requirements

Once an NDA or BLA is approved, a product will be subject to certain post approval requirements. For instance, the FDA closely regulates the post approval marketing and promotion of drugs, including standards and regulations for direct to consumer advertising, off label promotion, industry sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic safety reports is required following FDA approval of an NDA or BLA. The FDA also may require post marketing testing, known as Phase 4 testing, REMS and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging and labeling procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or

request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

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### Pediatric Information

Under the Pediatric Research Equity Act, a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration (i.e., that is subject to the Pediatric Research Equity Act) is required to submit an initial Pediatric Study Plan that includes pediatric studies and associated timelines (if warranted). The FDA may grant full or partial waivers, or deferrals, for submission of data for all pediatrics or specific age ranges or severities of disease.

The Best Pharmaceuticals for Children Act (“BPCA”) provides NDA holders a six month extension of any exclusivity, patent or non patent, for a drug if certain conditions are met. Conditions for exclusivity include the FDA’s determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric studies and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers.

### Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also encouraged to disclose the results of their clinical trials after completion, currently as part of FDA’s Clinical Data Summary Pilot Program. Competitors may use this publicly available information to gain knowledge regarding the progress of our programs.

### Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to regulations of other countries in which our clinical trials or commercial sales are conducted. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of countries outside of the United States before we can commence clinical trials or market products in those countries or areas. Regulatory authorities in certain countries outside of the United States require the submission of a clinical trial application (“CTA”) prior to the commencement of human clinical trials. In the European Union, for example, a CTA must be submitted to each country’s national health authority or via the Voluntary Harmonization Procedure (“VHP”) which includes member states planned for participation in the clinical trial. The European Union CTA process also requires review and approval by an independent ethics committee. Once the CTA is approved in accordance with VHP and/or individual countries’ requirements, clinical trial development may proceed. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country, and the time may be longer or shorter than that required for FDA approval.

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. This type of application is compulsory for medicines produced by biotechnology or those medicines intended to treat HIV, AIDS, cancer, neurodegenerative diseases, auto-immune and other immune dysfunctions, orphan (rare) diseases, viral diseases or diabetes and is optional for those medicines which are highly innovative. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization from one state may submit an application to the remaining member states. Within 90 days of receiving the applications and assessments report, each member state must decide whether to recognize approval. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on

all member states.

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### Anti Kickback, False Claims Laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry. These laws include, among others, anti kickback statutes, false claims statutes and other statutes pertaining to healthcare fraud and abuse. The federal healthcare program anti kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. The Patient Protection and Affordable Care Act, as amended (“PPACA”), amended the intent element of the federal anti kickback statute so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor.

### Other Federal and State Regulatory Requirements

The Centers for Medicare & Medicaid Services (“CMS”) has issued a final rule pursuant to the Physician Payments Sunshine Act, also known as section 6002 of the Affordable Care Act of 2010. It requires medical product manufacturers to disclose to the CMS any payments or other transfers of value made to physicians or teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Manufacturers were required to begin collecting information on August 1, 2013, with the first reports due March 31, 2014. The reported data is posted in searchable form on a public website maintained by CMS. Failure to submit required information may result in civil monetary penalties.

In addition, several states now require prescription drug companies to report expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual healthcare practitioners and entities in these states. Other states prohibit various other marketing related activities. Still other states require the posting of information relating to clinical studies and their outcomes. In addition, California, Connecticut, Nevada and Massachusetts require pharmaceutical companies to implement compliance programs and marketing codes. Several additional states are considering similar proposals. Some of the state laws are broader in scope than federal laws. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties.

### Reimbursement

Sales of any of our product candidates that are approved will depend, in part, on how our products are managed by third party payers, such as commercial insurance companies, pharmacy benefit managers and government health programs. Third party payers are responsible for managing overall pharmaceutical drug spending for their client membership and can employ a variety of means – including excluding a medicine from a formulary – to help control patient utilization. Third-party payers and their employer clients may also require patients to pay a high percentage of the list price of a medicine, which has been shown to negatively impact adherence to chronic medicines.

Additionally, the containment of healthcare costs has become a priority of the federal and state governments, and efforts to manage the prices of drugs have been a component of this effort. The U.S. federal government (including Congress), state legislatures and foreign governments have shown significant interest in implementing cost containment programs, including price controls, demonstration of cost effectiveness versus standard of care with

specified models, restrictions on reimbursement and requirements for mandatory substitution of therapeutically similar generic products. Adoption of price controls and cost containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could limit our net revenue and results of operation. If any of our products are approved and these third party payers do not consider our approved products to be clinically superior or cost effective compared to therapeutically similar therapies, they may not cover our approved products in their formularies, or, if covered, the amount of patient cost-sharing could deter initiation and/or subsequent adherence, which would affect our net profitability.

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The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (“MMA”) imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D of the MMA, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our approved products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payers may follow Medicare coverage policy and payment limitations in setting their own coverage policies. Any denials in coverage or high beneficiary cost-sharing that results from the MMA may result in similar treatment from non governmental payers.

The PPACA, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (collectively “ACA”), enacted in March 2010, had a significant impact on the health care industry. The ACA expanded coverage for the uninsured, while at the same time implementing measures to contain overall healthcare costs. We cannot predict the impact of the ACA on pharmaceutical companies, as many of the ACA reforms require the promulgation of detailed regulations implementing the statutory provisions, which has not yet occurred. Moreover, although the U.S. Supreme Court upheld the constitutionality of most of the ACA, some states have indicated that they intend to not implement certain sections of the ACA and the current presidential administration and certain members of the majority of the U.S. Congress have sought to repeal all or part of the ACA and implement a replacement program. For example, the so-called “individual mandate” was repealed as part of tax reform legislation adopted in December 2017, such that the shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code of 1986, as amended, will be eliminated beginning in 2019.

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

## Manufacturing and Supply

We use third-party contract manufacturing organizations (“CMOs”) for the production of all our clinical supply and commercial products. We do not have any in-house manufacturing facilities, and we plan to continue to rely on CMOs for our production needs for the foreseeable future. We have assembled a team of experienced employees and consultants to provide the necessary technical, quality and regulatory oversight over the CMOs with which we contract. We have commercial and development contracts and quality agreements with all CMOs for the manufacturing of drug substances, drug products and finished goods. For QBREXZA, we are adding manufacturing capacity at our current CMOs as appropriate, and we are adding additional CMOs to our manufacturing network in

anticipation of increased future commercial sales. We have mitigation plans in place to reduce the risk of supply interruption of QBREXZA, and we believe that we can support our commercial sales scenarios. However, the risks related to operating a global and virtual supply network remain, including but not limited to, risks related to regulatory action, labor disputes, single sources of supply and controlled temperature shipments.

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Pursuant to the terms of the Roche Agreement, Roche is responsible for the manufacture and supply to us of lebrikizumab drug substance, and Roche has the right to transfer its drug substance manufacture and supply responsibilities to us at any time. In November 2018, Roche provided us with notice of its election to transfer its drug substance manufacture and supply responsibilities to us. Pursuant to the terms of the Roche Agreement, the transfer must be completed within five years after delivery of the election notice. We do not currently have, nor do we plan to acquire, the infrastructure or capability to supply, manufacture or distribute clinical or commercial quantities of lebrikizumab drug substance. We are working with Roche to identify and qualify a contract manufacturer to manufacture and supply the lebrikizumab drug substance. For lebrikizumab, we manage the drug product production and device assembly at CMOs. All of the production steps for lebrikizumab are single sourced.

Failure of our CMOs to comply with statutory and regulatory requirements subjects them to possible legal or regulatory action, including warning letters, the seizure or recall of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations, and civil and criminal penalties. These actions could have a material impact on the availability of our products.

## Employees

As of December 31, 2018, we had 333 regular full time employees. From time to time, we also retain independent contractors to support our organization. Our employees are not represented by a labor union or covered by a collective bargaining agreement. We have not experienced any work stoppages, and we consider our relations with our employees to be good.

## Corporate Information

We were incorporated in the State of Delaware in August 2010 under the name Skintelligence, Inc. We changed our name to Dermira, Inc. in September 2011. Our principal executive offices are located at 275 Middlefield Road, Suite 150, Menlo Park, CA 94025, and our telephone number is (650) 421 7200. Our website address is [www.dermira.com](http://www.dermira.com). The information contained on, or that can be accessed through, our website is not a part of this Annual Report on Form 10 K.

## Available Information

Our website address is [www.dermira.com](http://www.dermira.com). The information contained on, or that can be accessed through, our website is not a part of this report. Investors should not rely on any such information in deciding whether to purchase our common stock. Our Annual Report on Form 10 K, Quarterly Reports on Form 10 Q, Current Reports on Form 8 K, reports filed pursuant to Section 16 under the Securities Exchange Act of 1934, as amended (“Exchange Act”), proxy and information statements and amendments to items filed pursuant to Sections 13(a), 14, 15(d) and 16 of the Exchange Act are filed with the U.S. Securities and Exchange Commission (“SEC”). We are subject to the informational requirements of the Exchange Act and file or furnish reports, proxy statements and other information with the SEC. The SEC maintains an Internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC at [www.sec.gov](http://www.sec.gov). Such documents and other information filed by us with the SEC are available free of charge on the Investor section of our website when such reports are available on the SEC’s website.

We webcast our earnings calls and certain events we participate in or host with members of the investment community on the “Investors” page of our website. Corporate governance information, including the charters for the committees of our board of directors, codes of business conduct and ethics and corporate governance guidelines, is also available on the “Investors” page of our website located at <http://investor.dermira.com>.

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In addition to SEC filings, press releases, public conference calls and webcasts, we use our website ([www.dermira.com](http://www.dermira.com)), LinkedIn page ([https://www.linkedin.com/company/dermira\\_inc](https://www.linkedin.com/company/dermira_inc)), corporate Instagram account ([https://www.instagram.com/dermira\\_inc/](https://www.instagram.com/dermira_inc/)) and corporate Twitter account (@DermiraInc) as channels of distribution of information about our company, our product and product candidates, our planned financial and other announcements, our attendance at upcoming investor and industry conferences and other matters. It is possible that the information we post on our website, LinkedIn page, Instagram account and our corporate Twitter account could be deemed material information. We may use these channels to comply with our disclosure obligations under

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Regulation FD. Therefore, investors should monitor our website, LinkedIn page, Instagram account and corporate Twitter account in addition to following our press releases, SEC filings, public conference calls and webcasts.

The contents of the websites referred to above are not incorporated into this report. Further, our references to the URLs for these websites are intended to be inactive textual references only.

## Executive Officers

The following table sets forth the names, ages as of February 26, 2019, and positions of our executive officers:

Name	Age	Position
Thomas G. Wiggans	67	Chief Executive Officer and Chairman of the Board
Eugene A. Bauer, M.D.	76	Chief Medical Officer and Director
Christopher M. Griffith	42	Chief Business and Strategy Officer
Andrew L. Guggenhime	50	Chief Financial Officer
Christopher Horan	52	Chief Technical Operations Officer
Lori Lyons-Williams	41	Chief Commercial Officer
Luis C. Peña	56	Chief Development Officer

Thomas G. Wiggans. Mr. Wiggans founded our company in August 2010, has served as our Chief Executive Officer and a member of our board of directors since August 2010 and has served as the Chairman of our board of directors since April 2014. He currently serves on the board of directors of Annexon Biosciences, Inc., a privately-held biotechnology company. Mr. Wiggans has also served on the boards of various industry organizations, educational institutions and private and public companies, including service on the boards of directors of Onyx from March 2005 until its acquisition by Amgen in October 2013, Sangamo Biosciences from June 2008 until June 2012, Somaxon Pharmaceuticals, Inc. from June 2008 until May 2012 and as Chairman of the board of directors of Excaliard Pharmaceuticals, Inc. from October 2010 until its acquisition by Pfizer in December 2011. From October 2007, Mr. Wiggans served as Chairman of the board of directors of Peplin and in August 2008, he became its Chief Executive Officer, serving in these positions until Peplin's acquisition by LEO Pharma in November 2009. Previously, Mr. Wiggans served as Chief Executive Officer of Connetics from 1994, and as Chairman of the board of directors of Connetics from January 2006, and he served in these positions until December 2006 when Connetics was acquired by Stiefel Laboratories. From 1992 to 1994, Mr. Wiggans served as President and Chief Operating Officer of CytoTherapeutics Inc., a biotechnology company. From 1980 to 1992, Mr. Wiggans served at Ares Serono S.A. in various management positions including President of its U.S. pharmaceutical operations and Managing Director of its U.K. pharmaceutical operations. Mr. Wiggans began his career with Eli Lilly. In addition, Mr. Wiggans is a member of the board of directors of the Biotechnology Innovation Organization and is a member of the board of trustees of the University of Kansas Endowment Association. Mr. Wiggans holds a B.S. in pharmacy from the University of Kansas and an M.B.A. from Southern Methodist University.

Eugene A. Bauer, M.D. Dr. Bauer founded our company in August 2010, has served as a member of our board of directors since August 2010 and has served as our Chief Medical Officer since October 2011. From February 2010 to June 2012, Dr. Bauer served on the board of directors of Vysteris, Inc. From June 2006, Dr. Bauer served as a member of board of directors of Peplin, Inc., a biotechnology company, and in October 2008, he became its President and Chief Medical Officer, and he served in these positions until Peplin's acquisition by LEO Pharma A/S in November 2009. From November 2004 to October 2008, Dr. Bauer was Chief Executive Officer of Neosil Inc., a dermatology company that was acquired by Peplin in October 2008. In 1993, Dr. Bauer co founded Connetics Corporation, a biotechnology company, where he served as a member of the board of directors until October 2005. Dr. Bauer served as Dean of the Stanford University School of Medicine from 1995 to 2001 and as Chair of the Department of

Dermatology at the Stanford University School of Medicine from 1988 to 1995. Dr. Bauer is a Lucy Becker Professor, Emeritus, in the School of Medicine at Stanford University, a position he has held since 2002. In addition, he is a member of the boards of directors of Aevi Genomic Medicine, Inc. (formerly Medgenics, Inc.), First Wave Technologies, Inc. and Kadmon Corporation, LLC. Dr. Bauer also previously served as a member of the boards of directors of Cerecor, Inc., Dr. Tattoff, Inc., Protalex, Inc., PetDRx, Inc., Arbor Vita Corp., Patient Safety Technologies, Inc., MediSync Bioservices and Modigene Inc. (later re named PROLOR Biotech, Inc.). Dr. Bauer was a U.S. National Institutes of Health (“NIH”) funded investigator for 25 years and has served on review groups for the NIH. Dr. Bauer has been elected to several societies, including the National



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Academy of Medicine of the United States, and currently serves as a director of the American Dermatological Association, Inc. Dr. Bauer received a B.S. in medicine and an M.D. from Northwestern University.

Christopher M. Griffith founded our company in August 2010 and has served as our Chief Business and Strategy Officer since May 2018, after previously serving as our Senior Vice President of Corporate Development and Strategy since January 2017, Vice President of Corporate Development and Strategy from August 2011 to January 2017, and our Head of Corporate Development and Strategy from September 2010 to August 2011. From July 2005 to September 2010, Mr. Griffith worked in corporate development at Gilead Sciences, Inc., a research-based biopharmaceutical company, most recently as Associate Director of Corporate Development. From May 2004 to August 2004, Mr. Griffith worked in the bio oncology strategy group at Genentech, Inc., a biotechnology company (“Genentech”). From 2001 to 2003, Mr. Griffith worked at Bay City Capital. Mr. Griffith received B.S. and M.S. degrees in biological sciences from Stanford University and an M.B.A. degree from Harvard Business School.

Andrew L. Guggenhime has served as our Chief Financial Officer since April 2014. Mr. Guggenhime also served as our Chief Operating Officer from April 2014 until May 2018. From September 2011 to April 2014, Mr. Guggenhime served as Chief Financial Officer for CardioDx, Inc., a molecular diagnostics life sciences company, and as a member of the CardioDx board of directors from April 2014 until July 2016. From September 2010 to April 2011, Mr. Guggenhime served as Chief Financial Officer for Calistoga Pharmaceuticals, Inc., a biotechnology company acquired in April 2011 by Gilead. From December 2008 to June 2010, Mr. Guggenhime served as Senior Vice President and Chief Financial Officer for Facet Biotech Corporation, a biotechnology company acquired in April 2010 by Abbott Laboratories. Facet Biotech Corporation was spun off from PDL BioPharma, Inc., a biopharmaceutical company, at which Mr. Guggenhime served as Chief Financial Officer from April 2006 to December 2008. From October 2000 to March 2006, Mr. Guggenhime served as Senior Vice President and Chief Financial Officer for Neoforma, Inc., a provider of supply chain management solutions for the healthcare industry, and from January to October 2000 he served as its Vice President, Corporate Development. Mr. Guggenhime began his career in financial services at Merrill Lynch & Co. and Wells Fargo & Company. He currently serves on the board of directors of Metacrine, Inc., a privately held biotechnology company. Mr. Guggenhime holds an M.B.A. from the J.L. Kellogg Graduate School of Management at Northwestern University and a B.A. in international politics and economics from Middlebury College.

Christopher Horan has served as our Chief Technical Operations Officer since April 2018. Prior to joining Dermira, Mr. Horan served approximately 14 years at Genentech, most recently as Senior Vice President of Product and Global Supply Chain Management for Roche Pharmaceuticals from May 2013 to March 2018. Mr. Horan also served as Vice President of TechOps Procurement for Roche Pharmaceuticals from July 2011 to May 2013 and Vice President of North American Supply Chain for Genentech from January 2007 to July 2011. Prior to this, he held various other positions within the operational excellence, procurement, supply chain and technical operations functions at Genentech. From 1988 to 2004, Mr. Horan worked in global roles across the engineering, manufacturing and operational excellence functions at Merck & Company, a pharmaceutical company. Mr. Horan holds a B.E. in engineering from The Stevens Institute of Technology.

Lori Lyons-Williams has served as our Chief Commercial Officer since December 2016. Prior to joining Dermira, Ms. Lyons-Williams served 15 years in various positions within the sales and marketing organization at Allergan plc, a pharmaceutical company, most recently as Vice President, Sales & Marketing for the Urology franchise from January 2014 to August 2016. In previous roles within Allergan, she served as Product Director for Allergan’s medical dermatology brands and also held senior-level positions on the Aczone and Botox marketing teams. Ms. Lyons-Williams began her career as a pharmaceutical sales representative at Johnson & Johnson. She currently serves as a director and Vice Chair of the National Association for Continence, a non-profit organization. She holds an M.B.A. from the Carlson School of Management of the University of Minnesota and a B.A. in interdisciplinary studies from Virginia Polytechnic Institute and State University.



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Luis C. Peña is a co-founder and has served as our Chief Development Officer since February 2016, after previously serving in various roles as our Executive Vice President of Product Development and Vice President of Product Development since June 2011. From November 2010 to June 2011, Mr. Peña served as a consultant to our company. Mr. Peña served as Vice President, Head of Global Prescription Development at Stiefel, a GSK company, from January 2010 to March 2011 and, from January 2007 to December 2009, Mr. Peña served as Senior Vice President Portfolio Planning and Management at Stiefel, prior to its acquisition by GlaxoSmithKline LLC. From 2005 to 2007, Mr. Peña served as Vice President of Portfolio Planning and Management of Connetics. From 2001 to 2005, Mr. Peña served as Vice President of Product Development of Nuvelo, Inc., a biopharmaceutical company. Previously, Mr. Peña served as Senior Director of Project Planning and Management for Theravance, Incorporated, a pharmaceutical company, and held various positions in manufacturing, research and development at Genentech. Mr. Peña currently serves as an advisor to the SPARK program for the Stanford University School of Medicine where he has been an advisor since 2012. Mr. Peña holds a B.S. in biochemistry from San Francisco State University.

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ITEM 1A. RISK FACTORS

RISK FACTORS

Our operations and financial results are subject to numerous risks and uncertainties, including those described below, which may have a material and adverse effect on our business, results of operations, cash flows, financial conditions, and the trading price of our common stock. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. You should consider these risks and uncertainties carefully, together with all of the other information included or incorporated by reference in this Annual Report on Form 10 K. If any of the following risks actually occur, our business, financial condition, results of operations and future prospects could be materially and adversely affected. In that event, the market price of our stock could decline, and you could lose part or all of your investment.

Risks Related to Commercialization of QBREXZA™ (glycopyrronium) Cloth

QBREXZA™ (glycopyrronium) cloth is our only approved product and the success of our business is dependent on its successful commercialization.

Our product, QBREXZA™ (glycopyrronium) cloth (“QBREXZA”), was recently approved by the U.S. Food and Drug Administration (“FDA”) for the topical treatment of primary axillary hyperhidrosis in adult and pediatric patients nine years of age and older and became available in pharmacies nationwide on October 1, 2018. The success of our business will depend on the successful commercialization of QBREXZA. The commercial success of QBREXZA will depend on a number of factors, including the following:

- the effectiveness of our sales team and our ability to scale our distribution capabilities (see also “—We recently built a team of sales representatives and our distribution capabilities. If we are unable to establish effective sales and distribution capabilities on our own or through third parties, we will be unable to successfully commercialize QBREXZA or generate product sales.”);
- the availability of formulary coverage and adequate reimbursement for QBREXZA (see also “—Our commercial success may be severely hindered if patients do not have access to our approved product from their insurers without undue restriction.”);
- the ability and willingness of patients to pay for QBREXZA (see also “—Our operating results and liquidity needs could be negatively affected by market fluctuations and economic downturn.”);
- acceptance by physicians, payers and patients of the benefits, safety and efficacy of QBREXZA, including relative to alternative and competing treatments (see also “—QBREXZA may fail to achieve the broad degree of physician and patient adoption and use necessary for commercial success.”);
- a continued acceptable safety profile of QBREXZA (see also “—QBREXZA may cause undesirable side effects or have other unexpected properties that could limit its commercial profile, result in post-approval regulatory action or expose us to product liability claims, any of which may adversely impact our business, financial condition, operating results and prospects.”);
- our ability to successfully obtain the substances and materials used in QBREXZA from third parties and to have finished product manufactured by third parties in accordance with regulatory requirements and in sufficient quantities for sale (see also “—Risks Related to Our Dependence on Third Parties”);
- our ability to ensure compliance with federal and state healthcare laws and regulations (see also “—Our employees, independent contractors, principal investigators, consultants, vendors, CROs, distributors, prescribers and any partners with which we may collaborate may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our business.” and “—We may also be subject to healthcare laws, regulation and enforcement and our failure to comply with those laws could adversely affect our business, operations and financial condition.”); and



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our ability to establish and enforce intellectual property rights in and to QBREXZA and avoid third-party patent interference or intellectual property infringement claims (see also “—Risks Related to Our Intellectual Property”). If we do not achieve one or more of these factors, many of which are beyond our control, in a timely manner or at all, we could experience significant delays or an inability to commercialize our product, increase sales and generate revenue, which would harm our business, financial condition, operating results and prospects.

We recently built a team of sales representatives and our distribution capabilities. If we are unable to maintain effective sales and distribution capabilities on our own or through third parties, we will be unable to successfully commercialize QBREXZA or generate product sales.

To achieve commercial success, we must effectively maintain our commercial infrastructure, including our sales and distribution capabilities, as well as continue to expand our organization cross-functionally to enable us to execute on our commercialization goals. Factors that may inhibit our efforts to successfully commercialize QBREXZA through our own sales organization include:

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

There are significant risks involved in managing a sales organization, including our ability to retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales personnel and effectively manage a geographically dispersed sales team. We may also choose to collaborate with third parties that have direct sales forces and established distribution systems to augment 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 QBREXZA. Even if we are able to enter into such arrangements, we will likely have little control over these third parties, and any such third party may fail to devote the necessary resources and attention to sell and market our product effectively. Any failure in our ability to maintain our commercial infrastructure and sales and distribution capabilities would adversely impact the commercialization of our product. The inability to successfully commercialize our product, either on our own or through collaborations with one or more third parties, would harm our business, financial condition, operating results and prospects.

We have contracted with a third-party logistics company to warehouse QBREXZA and distribute it to wholesalers, distributors, pharmacies, hospitals and other drug suppliers that will ultimately distribute our product directly to patients. Our third-party logistics company also provides billing, collection and returns services. This distribution network requires significant coordination with our market access, finance, quality and technical operations teams. Failure to maintain our contracts with our third-party logistics company, wholesalers, distributors, pharmacies, hospitals or other drug suppliers, or the inability or failure of any of them to adequately perform under the contracts, could negatively impact the distribution of our product. Failure to coordinate financial systems could also negatively impact our ability to accurately report and forecast product sales. If we are unable to effectively manage the distribution process, sales of QBREXZA could be severely compromised and our business, financial condition, operating results and prospects would be harmed.

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Our commercial success may be severely hindered if patients do not have access to QBREXZA from their insurers without undue restriction.

The availability of formulary coverage and adequate reimbursement from private third-party payers such as pharmacy benefit managers and commercial insurers, and to a lesser degree, governmental healthcare programs, such as Medicare and Medicaid, is critical to market acceptance and commercial success of QBREXZA, which is available only by prescription. Timely coverage and acceptable patient cost-sharing tiers for our product may be adversely affected by a number of factors, including but not limited to, increasing and intense pressure from political, social, competitive and other sources to reduce drug unit costs or limit changes in list price; changes in federal, state or foreign government regulations or private third-party payers' reimbursement policies; consolidation and increasing assertiveness of commercial payers seeking net price reduction via drug rebates and other forms of discounts linked to the placement of QBREXZA on their formularies; and the imposition of restrictions on access or coverage of particular drugs or pricing determined based on perceived pharmacoeconomic value.

A trend in the healthcare industry is cost containment. Third-party payers are developing increasingly sophisticated methods of controlling healthcare costs by, among other methods, limiting or preventing (via formulary exclusion) coverage for particular medications, requiring drug companies to provide them with varying levels of discounts from list prices and challenging the value of list prices charged for medical products. Coverage decisions may depend upon the size of a patient population, perceptions of clinical efficacy and economic standards that may disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

Although private third-party payers in the United States tend to follow Medicare reimbursement policies for products which are administered in a hospital or physician office setting, no uniform policy of pharmacy benefit coverage and reimbursement for drug products exists among third-party payers. Therefore, coverage and reimbursement for drug products adjudicated in a pharmacy benefit setting can differ significantly across payers. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product to each third-party payer separately, with no assurance that coverage will be obtained.

In addition, the market for QBREXZA will depend significantly on access to third-party payers' drug formularies, or lists of medications for which third-party payers provide coverage and impose patient out-of-pocket cost sharing limits. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payers may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other therapeutically similar alternative is available.

Third-party payers may also seek additional evidence, beyond the data required to obtain regulatory approval, demonstrating clinical benefits and value in specific patient populations before covering our product for those patients. This increased requirement is seen in particular with dermatology products that are perceived by payers to treat so-called lifestyle conditions. If third-party payers believe QBREXZA does not demonstrate sufficient value, they may not cover QBREXZA or may limit access to QBREXZA.

Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payers to reimburse all or part of the costs of their prescription drugs. Even if we obtain favorable coverage for our product, the patient may be required to pay co-payments or co-insurance they find unacceptably high. Patients may be unlikely to use QBREXZA unless a significant portion of the cost of our product is reimbursed through insurance coverage or reduced through the use of our savings card program.

Our inability to promptly obtain insurance coverage, profitable reimbursement rates or access to third-party payers' drug formularies from private payers and, to a smaller degree, government-funded health insurance for our product, could have a material adverse effect on our business, financial condition, operating results and prospects.



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QBREXZA may fail to achieve the broad degree of physician and patient adoption and use necessary for commercial success.

The commercial success of QBREXZA will depend significantly on the broad adoption and use of the product by physicians and patients for the approved indication. The degree and rate of physician and patient adoption of our product will depend on a number of factors, including:

- patient demand for an approved product that treats primary axillary hyperhidrosis;
- our ability to successfully compete with existing therapies, some of which are widely known and accepted by physicians and patients, including demonstrating that the relative cost, safety and efficacy of QBREXZA provides an attractive alternative to the existing therapies;
- the availability of formulary coverage and adequate reimbursement from private third-party payers for QBREXZA;
- the cost of treatment with QBREXZA in relation to alternative treatments and patients' willingness to pay for the product;
- acceptance by physicians, major operators of clinics and patients of QBREXZA as a safe and effective treatment;
- physician and patient willingness to adopt and prescribe a new therapy over other available therapies to treat primary axillary hyperhidrosis;
- patients' perception of primary axillary hyperhidrosis as a condition for which medical treatment may be appropriate and a prescription therapy may be available;
- overcoming any biases physicians or patients may have toward particular therapies for the treatment of primary axillary hyperhidrosis;
- proper training and administration of QBREXZA by physicians and medical staff;
- patients properly using QBREXZA as instructed;
- patient satisfaction with the results and administration of QBREXZA and overall treatment experience;
- the willingness of patients to pay for QBREXZA relative to other discretionary items, especially during economically challenging times;
- the revenue and profitability that QBREXZA may offer a physician as compared to alternative therapies;
- the prevalence and severity of side effects from the use or potential misuse of QBREXZA;
- limitations or warnings contained in the FDA-approved labeling of QBREXZA;
- the effectiveness of our sales, marketing and distribution efforts;
- adverse publicity about QBREXZA or favorable publicity about competitive products;
- potential product liability claims;
- our ability to effectively manage our third-party supply and manufacturing operations while increasing production capabilities for QBREXZA to commercial levels; and
- our ability to manage our operations to effectively support our commercialization activities.

In connection with the commercial launch of QBREXZA, we implemented a savings card program to provide assistance to eligible patients with out-of-pocket costs, such as deductibles, co-insurance and co-payments, for the patient's usage of QBREXZA. Changes to or elimination of the savings card program could adversely affect the frequency with which physicians prescribe QBREXZA, the availability of QBREXZA at pharmacies and the demand for and use of QBREXZA by patients.

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If QBREXZA fails to achieve the broad degree of physician, patient and payer adoption necessary for commercial success, our operating results and financial condition will be adversely affected, which may delay, prevent or limit our ability to generate revenue and continue our business.

QBREXZA may cause undesirable side effects or have other unexpected properties that could limit its commercial profile, result in post-approval regulatory action or expose us to product liability claims, any of which may adversely impact our business, financial condition, operating results and prospects.

If we or others identify undesirable side effects or other previously unknown problems caused by QBREXZA or other products with the same or related active ingredients, a number of potentially negative consequences could result, including:

- regulatory authorities may withdraw their approval of QBREXZA;
- we could be sued and held liable for harm caused to patients (see also “—We may face product liability exposure, and if successful claims are brought against us, we may incur substantial liability if our insurance coverage for those claims is inadequate.”);
- regulatory authorities may require a recall of QBREXZA or we or our potential partners may voluntarily recall the product (see also “—We or our current and prospective partners may be subject to product recalls in the future that could harm our brand and reputation and could negatively affect our business.”);
- regulatory authorities may require the addition of warnings or contraindications in the product labeling, narrowing of the indication in the QBREXZA label or field alerts to physicians and pharmacies;
- we may be required to institute a risk evaluation and mitigation strategy;
- we may have limitations on how we promote QBREXZA;
- we may be required to change the way QBREXZA is administered or modify the product in some other way;
- the FDA or applicable foreign regulatory authority may require additional clinical trials or costly post-marketing testing and surveillance to monitor the safety or efficacy of QBREXZA;
- sales of QBREXZA may decrease significantly; and
- our brand and reputation may suffer.

Any of the above events resulting from undesirable side effects or other previously unknown problems could prevent us or our potential partners from achieving or maintaining market acceptance of QBREXZA and could substantially increase our costs, which may adversely affect our business, financial condition, operating results and prospects.

We may face product liability exposure, and if successful claims are brought against us, we may incur substantial liability if our insurance coverage for those claims is inadequate.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and the commercialization of QBREXZA. This risk exists even if a product is approved for commercial sale by the FDA and manufactured in facilities licensed and regulated by the FDA or an applicable foreign regulatory authority. QBREXZA and our past and current product candidates were designed to affect important bodily functions and processes. Any side effects, manufacturing defects, failure to follow instructions, misuse or abuse associated with our product or product candidates could result in injury to a patient or even death. We cannot offer any assurance that we will not face product liability suits in the future, nor can we provide assurances that our insurance coverage will be sufficient to cover our liability under any such cases.

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In addition, a liability claim may be brought against us even if our product or product candidates merely appear to have caused an injury. Product liability claims may be brought against us by, among others, consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our product or product candidates. If we cannot successfully defend ourselves against product liability claims, we will incur substantial liabilities and reputational harm. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- the inability to commercialize our product or product candidates;
- decreased demand for our product or product candidates;
- product recall or withdrawal from the market or labeling, marketing or promotional restrictions;
- withdrawal of clinical trial participants;
- decreased enrollment rates of clinical trial participants;
- termination of clinical trial sites or entire clinical trial programs;
- impairment of our business reputation;
- substantial costs of any related litigation or similar disputes;
  - distraction of management's attention and other resources from our primary business;
- substantial monetary awards to patients or other claimants against us that may not be covered by insurance; or
- loss of revenue.

Large judgments have been awarded in class action or individual lawsuits based on drugs that had anticipated or unanticipated side effects. Although we have obtained product liability insurance coverage, our insurance coverage may not be sufficient to cover all of our product liability related expenses or losses and may not cover us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and, in the future, we may not be able to maintain insurance coverage at a reasonable cost, in sufficient amounts or upon adequate terms to protect us against losses due to product liability. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and could harm our business, financial condition, operating results and prospects.

If we are found to have improperly promoted off-label uses of QBREXZA, or if physicians misuse our product or use our product off-label, we may become subject to prohibitions on the sale or marketing of our product, product liability claims and significant fines, penalties and sanctions, and our brand and reputation could be harmed.

The FDA and other regulatory agencies strictly regulate the marketing and promotional claims that are made about drug and biologic products. In particular, a product may not be promoted for uses or indications that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling and comparative safety or efficacy claims cannot be made without direct comparative clinical data. For example, although QBREXZA may appeal to individuals who have not been diagnosed with primary axillary hyperhidrosis or suffer from other forms of hyperhidrosis, we are able to promote it only for primary axillary hyperhidrosis. If we are found to have promoted off-label uses of our product, we may receive warning or untitled letters and become subject to significant criminal and civil liability, which would materially harm our business. Both federal and state governments have levied large civil and criminal fines against companies for alleged improper off-label promotion and have enjoined several companies from engaging in off-label promotion.

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If we become the target of such an investigation or prosecution based on our marketing and promotional practices, we could face similar sanctions, which would materially harm our business. In addition, management's attention could be diverted from our business operations, significant legal expenses could be incurred and our brand and reputation could be damaged. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we are deemed by the FDA to have engaged in the promotion of our product for off-label uses, we could be subject to FDA regulatory or enforcement actions, including the issuance of an untitled letter, a warning letter, injunction, seizure, civil fine or criminal penalties. It is also possible that other federal, state or foreign enforcement authorities might take action if they consider our business activities to constitute promotion of an off-label use, which could result in significant penalties, including criminal, civil or administrative penalties, damages, fines, disgorgement, exclusion from participation in government healthcare programs and the curtailment or restructuring of our operations.

We cannot, however, prevent a physician from prescribing our product outside of its approved indication when in the physician's independent professional medical judgment he or she deems appropriate. Physicians or patients may also misuse our product or use improper techniques, potentially leading to adverse results, side effects or injury, which may lead to product liability claims. If our product is misused or used with improper technique, we may become subject to costly litigation by physicians or their patients. See also "—We may face product liability exposure, and if successful claims are brought against us, we may incur substantial liability if our insurance coverage for those claims is inadequate." Furthermore, the use of our product for indications other than those approved by the FDA may not effectively treat such conditions, which could adversely impact patient satisfaction with the results and administration of QBREXZA and harm our reputation among physicians and patients.

We rely completely on third parties to supply, manufacture and distribute drug supplies for QBREXZA, including certain sole-source suppliers and manufacturers.

We do not currently have, nor do we plan to acquire, the infrastructure or capability to supply, manufacture or distribute commercial quantities of QBREXZA. Our ability to commercially supply QBREXZA depends, in part, on our ability to successfully manufacture drug substance and other substances and materials used in QBREXZA from third parties and to have the finished product manufactured by third parties in accordance with regulatory requirements and in sufficient quantities for sale. If we fail to develop and maintain supply relationships with these third parties, we may be unable to successfully commercialize QBREXZA.

We rely and will continue to rely on certain third parties as the sole source of the materials they supply or the finished products they manufacture. For example, we are dependent on our current suppliers of the nonwoven material and pouchstock in QBREXZA. Any of our existing suppliers or manufacturers may:

- fail to supply us with product on a timely basis or in the requested amount due to unexpected damage to or destruction of facilities or equipment or otherwise;
- fail to increase manufacturing capacity and produce drug product and components in larger quantities and at higher yields in a timely or cost-effective manner, or at all, to sufficiently meet our commercial needs;
- be unable to meet our production demands due to issues related to their reliance on sole-source suppliers and manufacturers;
- supply us with product that fails to meet regulatory requirements;
  - become unavailable through business interruption or financial insolvency;
- lose regulatory status as an approved source;
- be unable or unwilling to renew current supply agreements when such agreements expire on a timely basis, on acceptable terms or at all; or
- discontinue production or manufacturing of necessary drug substances or products.



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In the event of any of the foregoing, if we do not have an alternative supplier or manufacturer in place, we would be required to expend substantial management time and expense to identify, qualify and transfer processes to alternative suppliers or manufacturers. Transferring technology to other sites may require additional processes, technologies and validation studies, which are costly, may take considerable amounts of time, may not be successful and, in most cases, require review and approval by the FDA and foreign regulatory authorities. Any need to find and qualify new suppliers or manufacturers could delay production of QBREXZA indefinitely, adversely impact our ability to market QBREXZA and adversely affect our business. There can be no assurance that replacements would be available to us on a timely basis, on acceptable terms or at all. Additionally, we and our manufacturers do not currently maintain significant inventory of drug substances and other materials. Any interruption in the supply of a drug substance or other material or in the manufacture of QBREXZA could have a material adverse effect on our business, financial condition, operating results and prospects.

Additionally, although we are ultimately responsible for ensuring compliance with regulatory requirements such as current good manufacturing practices (“cGMPs”), we are dependent on our contract suppliers and manufacturers for day-to-day compliance with cGMP for production of both drug substances and finished products. Facilities used by our contract suppliers and manufacturers to produce the drug substances and materials or finished products for commercial sale must pass inspection and be approved by the FDA and other relevant regulatory authorities. A number of our contract suppliers and manufacturers must comply with cGMP requirements enforced by the FDA through its facilities inspection program and review of submitted technical information. If the safety of QBREXZA is compromised due to a failure to adhere to applicable laws or for other reasons, we may not be able to successfully commercialize our product and we may be held liable for injuries sustained as a result. In addition, the manufacturing facilities of certain of our suppliers are located outside of the United States. This may give rise to difficulties in importing our product into the United States or other countries as a result of, among other things, regulatory agency approval requirements, taxes, tariffs, local import requirements such as import duties or inspections, incomplete or inaccurate import documentation or defective packaging. Any of these factors could adversely impact our ability to effectively commercialize QBREXZA.

QBREXZA will be subject to ongoing and continued regulatory review. Failure to comply with applicable regulatory requirements could have a material adverse impact on our business.

We are subject to ongoing FDA obligations and continued regulatory review with respect to, among other things, the manufacturing, processing, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for QBREXZA. These requirements include submissions of safety and other post-marketing information and reports and registration, as well as continued compliance with cGMP requirements and with the FDA’s good clinical practice (“GCP”).

In addition, manufacturers of drug and biologic products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where, or processes by which, the product is manufactured, a regulatory agency may impose restrictions on that product or us, including requesting that we initiate a product recall, or requiring notice to physicians, withdrawal of the product from the market or suspension of manufacturing.

If we, our product or product candidates or the manufacturing facilities for our product or product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- impose restrictions on the marketing or manufacturing of the product, suspend or withdraw product approvals or revoke necessary licenses;

mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;

• require us or our partners to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;

• issue warning letters, show cause notices or untitled letters describing alleged violations, which may be publicly available;

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- commence criminal investigations and prosecutions;
- impose injunctions, suspensions or revocations of necessary approvals or other licenses;
- impose other civil or criminal penalties;
- suspend any ongoing clinical trials;
- delay or refuse to approve pending applications or supplements to approved applications filed by us or our potential partners;
- refuse to permit drugs or precursor chemicals to be imported or exported to or from the United States;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or require us or our partners to initiate a product recall.

The regulations, policies or guidance of the FDA and other applicable government agencies may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post-approval activities. We cannot predict the likelihood, nature or extent of adverse government regulations that may arise from future legislation or administrative action, either in the United States or abroad. If we are not able to achieve and maintain regulatory compliance, we may not be permitted to market our product candidates, which would adversely affect our ability to generate revenue and achieve or maintain profitability.

We or our current and prospective partners may be subject to product recalls in the future that could harm our brand and reputation and could negatively affect our business.

We or our current and prospective partners may be subject to product recalls, withdrawals or seizures if QBREXZA fails to meet specifications or is believed to cause injury or illness or if we are alleged to have violated governmental regulations including those related to manufacturing, labeling, promotion, sale or distribution. Any recall, withdrawal or seizure in the future could materially and adversely affect consumer confidence in our brand and lead to decreased demand for our product. In addition, a recall, withdrawal or seizure of QBREXZA would require significant management attention, would likely result in substantial and unexpected expenditures and would harm our business, financial condition, operating results and prospects.

### Risks Related to Development and Regulatory Approval of Our Product Candidates

Our business is dependent on the successful development and regulatory approval of our current and any future product candidates.

Our product candidate, lebrikizumab, is currently in Phase 2b development for the treatment of moderate-to-severe atopic dermatitis. We also have early-stage research and development programs in other areas of dermatology. The success of our business, including our ability to finance our company and generate additional revenue in the future, will depend on the successful development and regulatory approval of our current product candidate and any future product candidates we may in-license, acquire or develop. The clinical success of our current and any future product candidates will depend on a number of factors, including the following:

- the ability to raise additional capital on acceptable terms, or at all;
- timely completion of our clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors as well as our ability to timely recruit and enroll patients in our clinical trials, which may be delayed due to numerous factors, including the prevalence of other companies' clinical trials for their product candidates for the same or similar indications;
- whether we are required by the FDA or similar foreign regulatory agencies to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our current or any future product candidates;





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- acceptance of our proposed indications and primary endpoint assessments relating to the proposed indications of our current or any future product candidates by the FDA and similar foreign regulatory authorities;
  - our ability to demonstrate to the satisfaction of the FDA and similar foreign regulatory authorities the safety, efficacy and acceptable risk to benefit profile of our current or any future product candidates;
  - the prevalence, duration and severity of potential side effects experienced with our current or any future product candidates;
  - the timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities;
  - achieving and maintaining, and, where applicable, ensuring that our third-party contractors achieve and maintain, compliance with our contractual obligations and with all regulatory requirements applicable to our current or any future product candidates;
  - our ability to successfully obtain the substances and materials used in our current or any future product candidates from third parties and to have finished products manufactured by third parties in accordance with regulatory requirements and in sufficient quantities for preclinical and clinical testing;
  - the ability of third parties with whom we contract to manufacture clinical trial supplies of our current or any future product candidates, remain in good standing with regulatory agencies and develop, validate and maintain commercially viable manufacturing processes that are compliant with cGMP; and
  - a continued acceptable safety profile during clinical development of our current or any future product candidates.
- If we do not achieve one or more of these factors, many of which are beyond our control, in a timely manner or at all, we could experience significant delays or an inability to successfully complete and obtain regulatory approvals of our current or any future product candidates.

Clinical drug development is very expensive, time-consuming and uncertain. Our clinical trials may fail to adequately demonstrate the safety and efficacy of our current or any future product candidates, which could prevent or delay regulatory approval and commercialization.

Clinical drug development is very expensive, time-consuming and difficult to design and implement, and its outcome is inherently uncertain. Before obtaining regulatory approval for the commercial sale of a product candidate, we must demonstrate through clinical trials that a product candidate is both safe and effective for use in the target indication. Most product candidates that commence clinical trials are never approved by regulatory authorities for commercialization. The clinical trials for these product candidates may take significantly longer than expected to complete. In addition, we, any partner with which we currently or may in the future collaborate, the FDA, an institutional review board (“IRB”) or other regulatory authorities, including state and local agencies and counterpart agencies in foreign countries, may suspend, delay, require modifications to or terminate our clinical trials at any time, for various reasons, including:

- discovery of serious or unexpected toxicities or side effects experienced by study participants or other safety issues;
- lack of effectiveness of any product candidate during clinical trials or the failure of a product candidate to meet specified endpoints;
- slower than expected rates of subject recruitment and patient enrollment in clinical trials resulting from numerous factors, including the prevalence of other companies’ clinical trials for their product candidates for the same indication, such as atopic dermatitis;
- difficulty in retaining subjects who have initiated participation in a clinical trial but may withdraw at any time due to adverse side effects from the therapy, insufficient efficacy, fatigue with the clinical trial process or for any other reason;
- difficulty in obtaining IRB approval for studies to be conducted at each site;

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- delays in manufacturing or obtaining, or inability to manufacture or obtain, sufficient quantities of materials for use in clinical trials;
- inadequacy of or changes in our manufacturing process or the product formulation or method of delivery;
- changes in applicable laws, regulations and regulatory policies;
- delays or failure in reaching agreement on acceptable terms in clinical trial contracts or protocols with prospective contract research organizations (“CROs”), clinical trial sites and other third-party contractors;
- inability to add a sufficient number of clinical trial sites;
- uncertainty regarding proper dosing;
- failure of our CROs or other third-party contractors to comply with contractual and regulatory requirements or to perform their services in a timely or acceptable manner;
- failure by us, our employees, our CROs or their employees or any partner with which we may collaborate or their employees to comply with applicable FDA or other regulatory requirements relating to the conduct of clinical trials or the handling, storage, security and recordkeeping for drug and biologic products;
- scheduling conflicts with participating clinicians and clinical institutions;
- failure to design appropriate clinical trial protocols;
- inability or unwillingness of medical investigators to follow our clinical protocols;
- difficulty in maintaining contact with subjects during or after treatment, which may result in incomplete data; or
- insufficient data to support regulatory approval.

We or any partner with which we may collaborate may suffer significant setbacks in our clinical trials similar to the experience of a number of other companies in the pharmaceutical and biotechnology industries, even after receiving promising results in earlier trials. In the event that we or our potential partners abandon or are delayed in the clinical development efforts related to our current or any future product candidates, we may not be able to execute on our business plan effectively and our business, financial condition, operating results and prospects would be harmed. For example, in March 2018, we received results that the investigational treatment olumacostat glasaretil (formerly DRM01) for moderate-to-severe acne vulgaris did not meet the co-primary endpoints in its two Phase 3 pivotal trials (CLAREOS-1 and CLAREOS-2) in patients ages nine years and older notwithstanding earlier clinical trials. Based on these results, we have discontinued the development program. Furthermore, if we experience delays in the completion of, or if we terminate, any of our current or future clinical trials, our business, financial condition, operating results and prospects would be adversely affected.

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We have in the past relied and expect to continue to rely on third-party CROs and other third parties to conduct and oversee our clinical trials, other aspects of our product development and our regulatory submission process. If these third parties do not meet our requirements, conduct the trials as required or otherwise provide services as anticipated, we may not be able to satisfy our contractual obligations or obtain regulatory approval for, or successfully commercialize, our current or any future product candidates when expected or at all.

We have in the past relied and expect to continue to rely on third-party CROs and other third parties to conduct and oversee our clinical trials, other aspects of our product development and our regulatory submission process. We also rely upon various medical institutions, clinical investigators and contract laboratories to conduct our trials in accordance with our clinical protocols and all applicable regulatory requirements, including the FDA's regulations and GCPs, which are an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors, and state regulations governing the handling, storage, security and recordkeeping for drug and biologic products. These CROs and other third parties play a significant role in the conduct of our clinical trials, the subsequent collection and analysis of data from the clinical trials, the preparation for and submission of our filings with the FDA and comparable foreign regulatory authorities and the successful commercialization of our product.

We rely heavily on third parties for the execution of our clinical trials and preclinical studies, and control only certain aspects of their activities. We and our CROs and other third-party contractors are required to comply with GCP and good laboratory practice ("GLP") requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for products in clinical development. Regulatory authorities enforce these GCP and GLP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP and GLP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other regulatory authorities may require us to perform additional clinical trials before approving our or our partners' marketing applications. We cannot provide assurances that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials or preclinical studies complies with applicable GCP and GLP requirements. In addition, our clinical trials must generally be conducted with products produced under cGMP regulations. Our failure to comply with these regulations and policies may require us to repeat clinical trials, which would delay the regulatory approval process.

If any of our CROs or clinical trial sites terminate their involvement in our clinical trials for any reason, we may not be able to enter into arrangements with alternative CROs or clinical trial sites in a timely manner, or do so on commercially reasonable terms or at all. In addition, if our relationship with clinical trial sites is terminated, we may experience the loss of follow-up information on patients enrolled in our ongoing clinical trial unless we are able to transfer the care of those patients to another qualified clinical trial site. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and could receive cash compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, the integrity of the data generated at the applicable clinical trial site may be questioned by the FDA and comparable foreign regulatory authorities.

Additionally, the regulatory submission process for a product candidate is complex. We expect to rely on a third-party service provider for the preparation and submission of filings with the FDA and comparable foreign regulatory authorities for approval of our current and any future product candidates. If our relationship with such service provider is terminated prior to completion of our regulatory submission process, we may not be able to enter into an arrangement with an alternative service provider in a timely manner, or do so on commercially reasonable terms, and our submission may be substantially delayed.

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We are dependent on F. Hoffmann-La Roche Ltd and Genentech, Inc. (together, “Roche”) for the manufacture and supply of lebrikizumab drug substance. Roche has elected to transfer its manufacture and supply responsibilities to us and we have until November 2023 to engage a qualified contract manufacturer to manufacture and supply the drug substance. Any interruption in our supply may cause serious delays in the timing of our clinical trials, increase our costs and adversely impact our financial results.

Pursuant to the terms of our license agreement with Roche for the exclusive, worldwide rights to develop and commercialize lebrikizumab for, among other indications, atopic dermatitis (the “Roche Agreement”), Roche is responsible for the manufacture and supply to us of lebrikizumab drug substance and we are completely reliant upon Roche to provide us with adequate supply for our use. We may experience an interruption in supply if, among other reasons, we incorrectly forecast our supply requirements, Roche allocates supply to its own development programs, Roche incorrectly plans its manufacturing production or Roche is unable to manufacture lebrikizumab drug substance in a timely manner to match our development or commercial needs.

Additionally, the Roche Agreement provides that, subject to certain requirements, Roche has the right to transfer its drug substance manufacture and supply responsibilities to us at any time. We do not currently have, nor do we plan to acquire, the infrastructure or capability to supply, manufacture or distribute clinical or commercial quantities of lebrikizumab drug substance. In November 2018, Roche provided us with notice of its election to transfer its drug substance manufacture and supply responsibilities to us. Pursuant to the terms of the Roche Agreement, the transfer must be completed within five years after delivery of the election notice and we are responsible for the costs incurred in connection with the transfer and qualifying a contract manufacturer to manufacture and supply the lebrikizumab drug substance. There can be no assurance that a qualified contract manufacturer would be available to us on a timely basis, on acceptable terms or at all, or that a seamless transfer of technology would occur from Roche to the contract manufacturer. If we experience any interruption in the supply of lebrikizumab drug substance, our ability to timely supply our clinical sites would be adversely impacted, causing potentially serious delays in the timing of our clinical trials and substantially increased costs if trials need to be adjusted or re-performed.

We may be unable to obtain regulatory approval for our current or any of our future product candidates under applicable regulatory requirements. The FDA and foreign regulatory bodies have substantial discretion in the approval process, including the ability to delay, limit or deny approval of product candidates. The delay, limitation or denial of any regulatory approval would adversely impact our business and our operating results.

We may never obtain regulatory approval to commercialize our current or any future product candidates. The research, testing, manufacturing, safety surveillance, efficacy, quality control, recordkeeping, labeling, packaging, storage, approval, sale, marketing, distribution, import, export and reporting of safety and other post-market information related to our current and any future product candidates are subject to extensive regulation by the FDA and other regulatory authorities in the United States and in foreign countries, and such regulations differ from country to country. We are not permitted to market any of our current or any future product candidates in the United States until we receive approval of an NDA, biologics license application (“BLA”) or other applicable regulatory filing from the FDA. We are also not permitted to market our product or our current or any future product candidates in any foreign countries until we receive the requisite approval from the applicable regulatory authorities of such countries.

To gain approval to market a new drug, the FDA and foreign regulatory authorities must receive preclinical, clinical and chemistry, manufacturing and controls data that adequately demonstrate the safety, purity, potency, efficacy and compliant manufacturing of the product for the intended indication applied for in an NDA, BLA or other applicable regulatory filing. The development and approval of new drug products and biologic products involves a long, expensive and uncertain process. A delay or failure can occur at any stage in the process. A number of companies in the pharmaceutical and biopharmaceutical industry have suffered significant setbacks in clinical trials, including in Phase 3 clinical development, even after promising results in earlier preclinical studies or clinical trials. These

setbacks have been caused by, among other things, findings made while clinical trials were underway and safety or efficacy observations made in clinical trials, including previously unreported adverse events. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and the results of clinical trials by other parties may not be indicative of the results in trials we or our partners may conduct.

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The FDA and foreign regulatory bodies have substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of product candidates for many reasons, including:

- the FDA or the applicable foreign regulatory body may disagree with the design, implementation, choice of dose, analysis plans or interpretation of the outcome of one or more clinical trials;
- the FDA or the applicable foreign regulatory body may not deem a product candidate safe and effective for its proposed indication, or may deem a product candidate's safety or other perceived risks to outweigh its clinical or other benefits;
- the FDA or the applicable foreign regulatory body may not find the data from preclinical studies and clinical trials, including the number of subjects in the safety database, sufficient to support approval, or the results of clinical trials may not meet the level of statistical or clinical significance required by the FDA or the applicable foreign regulatory body for approval;
- the FDA or the applicable foreign regulatory body may disagree with our interpretation of data from preclinical studies or clinical trials performed by us or third parties, or with the interpretation of any partner with which we may collaborate;
- the data collected from clinical trials may not be sufficient to support the submission and approval of an NDA, BLA or other applicable regulatory filing;
- the FDA or the applicable foreign regulatory body may require additional preclinical studies or clinical trials;
- the FDA or the applicable foreign regulatory agency may identify deficiencies in the formulation, manufacturing, quality control, labeling or specifications of our current or any future product candidates;
  - the FDA or the applicable foreign regulatory agency may require clinical trials in pediatric patients in order to establish pharmacokinetics or safety for this more drug-sensitive population;
- the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional post-approval clinical trials;
- the FDA or the applicable foreign regulatory agency may grant approval but impose substantial and costly post-approval requirements;
- the FDA or the applicable foreign regulatory agency may approve our current or any future product candidates for a more limited indication or a narrower patient population than we originally requested;
  - the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of our current or any future product candidates;
- the FDA or the applicable foreign regulatory body may not approve of the manufacturing processes, controls or facilities of third-party manufacturers or testing labs with which we contract; or
- the FDA or the applicable foreign regulatory body may change its approval policies or adopt new regulations in a manner rendering our clinical data or regulatory filings insufficient for approval.

Of the large number of drugs, including biologics, in development, only a small percentage successfully complete the FDA or other regulatory approval processes and are commercialized. For example, our current and any future product candidates may not be approved by the FDA or applicable foreign regulatory agencies even though they meet specified endpoints in our clinical trials. The FDA or applicable foreign regulatory agencies may ask us to conduct additional costly and time-consuming clinical trials in order to obtain marketing approval or approval to enter into an advanced phase of development, or may change the requirements for approval even after such agency has reviewed and commented on the design for the clinical trials. Any delay in obtaining, or inability to obtain, applicable regulatory approval for any of our product candidates would delay or prevent commercialization of our current and any future product candidates and would harm our business, financial condition, operating results and prospects.

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We have never obtained approval of a BLA submission or equivalent foreign filing, and we may be unable to successfully do so for any of our current or any future product candidates. Failure to successfully prepare or obtain approval of a BLA or equivalent foreign filing in a timely manner for our current or any future product candidates could have a material adverse impact on our business and financial performance.

Obtaining approval of a BLA submission or equivalent foreign filing involves complicated processes. Although our employees have obtained approvals for BLAs in the past while employed at other companies, we as a company have not obtained approvals of BLAs or equivalent foreign filings. As a result, such activities may require more time and cost more than we anticipate. Failure to complete or obtain, or delays in completing or obtaining, approval of our BLA submission for our current or any future product candidates would prevent us from or delay us in commercializing the product candidate in the United States. The occurrence of any of the foregoing could have a material adverse impact on our business and financial performance.

We may conduct clinical trials for our current and any future product candidates outside the United States and the FDA and applicable foreign regulatory authorities may not accept data from such trials, which would likely result in additional costs to us and delay our business plan.

We have conducted, and may in the future choose to conduct, one or more of our clinical trials outside the United States. For example, our Phase 3 clinical program for glycopyrronium tosylate was conducted in multiple countries. Although the FDA or applicable foreign regulatory authority may accept data from clinical trials conducted outside the United States or the applicable jurisdiction, acceptance of such study data by the FDA or applicable foreign regulatory authority may be subject to certain conditions. Where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will not approve the application on the basis of foreign data alone unless those data are applicable to the U.S. population and U.S. medical practice; the studies were performed by clinical investigators of recognized competence; and the data are considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Many foreign regulatory bodies have similar requirements. In addition, such foreign studies would be subject to the applicable local laws of the foreign jurisdictions where the studies are conducted. There can be no assurance the FDA or applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or applicable foreign regulatory authority does not accept such data, it would likely result in the need for additional clinical trials, which would be costly and time-consuming and delay aspects of our business plan.

### Other Risks Related to Our Business and Financial Operations

We have had significant and increasing operating expenses and we will require substantial additional financing to achieve our goals, which we may not be able to obtain when needed and on acceptable terms, or at all. We have a history of losses, we have not generated any significant revenue from product sales and we may not be able to achieve or maintain profitability, which could cause our business and operating results to suffer.

We are a biopharmaceutical company with a limited operating history upon which investors can evaluate our business and prospects. QBREXZA, which became available in pharmacies nationwide on October 1, 2018, is our only product approved for commercialization. We have not generated any significant revenue from product sales. We are not profitable and have incurred losses in each year since we commenced operations in August 2010. We have incurred net losses of \$221.5 million, \$303.3 million and \$89.1 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had an accumulated deficit of \$745.0 million.

We have financed our operations primarily through the sale of equity securities and convertible debt securities. Since our inception, most of our resources have been dedicated to the development of our product candidates and, more



recently, preparation for and execution of the commercial launch of QBREXZA. The size of our future net losses will depend, in part, on our future expenses and our ability to generate revenue through future sales of QBREXZA, any future products and our current and potential future collaborations. Revenue from our current and potential future collaborations is uncertain because milestones or other contingent payments under our agreements may not be achieved or received.

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As of December 31, 2018, we had capital resources consisting of cash and investments of \$316.0 million. We will continue to expend substantial cash resources for the foreseeable future for the commercialization of QBREXZA and the clinical development of our current product candidate and development of any other indications and product candidates we may choose to pursue. These expenditures will include costs associated with any acquisition or in-license of products and product candidates, technologies or businesses, research and development, conducting preclinical studies, non-clinical studies and clinical trials, manufacturing and supply, regulatory submissions, preparing for potential commercial approvals and product launches, as well as marketing and selling any products approved for sale. In addition, other unanticipated costs may arise. Because the conduct and results of any clinical trial are highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our current and any future product candidates.

We believe that existing cash and investments on hand as of December 31, 2018 are sufficient to meet our anticipated cash requirements, excluding costs to conduct a potential Phase 3 program for lebrikizumab, to at least mid-2020 and to: continue to commercialize QBREXZA; complete and generate topline results from our ongoing Phase 2b dose-ranging study for lebrikizumab; and continue potential lifecycle management activities related to our product candidates. We have based these estimates, however, on assumptions that may prove to be wrong, and we could spend our available capital resources much faster than we currently expect or require more capital to fund our operations than we currently expect. See also “—Our future operating results are difficult to predict and may fluctuate significantly. Our gross-to-net estimates related to revenue recognition from product sales are difficult to estimate and if our estimates differ significantly from actual product sales, we will be required to record an adjustment in a subsequent period.” We will need to raise additional capital to fund our operations and continue to support our planned research and development and commercialization activities.

The amount and timing of our future funding requirements will depend on many factors, including:

- costs to maintain our infrastructure to continue our commercialization of QBREXZA;
- the cost of commercialization activities, including manufacturing, marketing, sales and distribution costs;
- the degree and rate of market acceptance of QBREXZA;
- the amount of revenue generated from future sales of QBREXZA;
- the timing, rate of progress and cost of any preclinical and clinical trials and other product development activities for our current and any future product candidates that we develop, in-license or acquire;
- the results of the clinical trials for our current and any future product candidates in the United States and any foreign countries;
- the timing of, and the costs involved in, FDA approval and any foreign regulatory approval of our current and any future product candidates, if at all;
- the number and characteristics of any additional future product candidates we develop or acquire;
- our ability to establish and maintain strategic collaborations, licensing, co-promotion or other arrangements and the terms and timing of such arrangements;
- costs under our third-party manufacturing and supply arrangements for QBREXZA and our current and any future product candidates we commercialize;
- costs and timing of completion of any additional outsourced commercial manufacturing or supply arrangements that we may establish;
- costs associated with the transfer of manufacturing and supply responsibilities for lebrikizumab drug substance (see “—We are dependent on Roche for the manufacture and supply of lebrikizumab drug substance. Roche has elected to transfer its manufacture and supply responsibilities to us and we have until November 2023 to engage a qualified contract manufacturer to manufacture and supply the drug substance. Any interruption in our supply may cause serious delays in the timing of our clinical studies, increase our costs and adversely impact our financial results.”);

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- costs of preparing, filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights associated with QBREXZA and our current and any future product candidates, including post-grant challenges or opposition to third-party patent claims;
- costs associated with prosecuting or defending any litigation that we may become involved in and any damages payable by us that result from such litigation;
- costs associated with defending any government investigations or enforcement actions including legal costs and fines;
- costs associated with any product recall that could occur;
- costs of operating as a public company;
- the emergence, approval, availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing products or treatments;
- costs associated with any acquisition or in-license of products and product candidates, technologies or businesses; and
- personnel, facilities and equipment requirements.

We cannot be certain that additional funding will be available on acceptable terms, or at all. Any future debt financing into which we enter may impose upon us covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, redeem our stock, make certain investments and engage in certain merger, consolidation or asset sale transactions. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe that we have sufficient funds for our current or future operating plans.

In order to fund the development and potential commercialization of our current and any future product candidates, we may also need to enter into collaboration agreements with pharmaceutical and biotechnology companies. Our ability to establish and maintain these collaborations is highly uncertain and subject to a number of variables. Under these arrangements, we may be responsible for substantial costs in connection with the clinical development, regulatory approval or the commercialization of a partnered product candidate. Furthermore, the payments we could receive from our potential collaboration partners may be subject to numerous conditions and may ultimately be insufficient to cover the cost of this development and commercialization.

If we are unable to raise additional capital when required or on acceptable terms, we may be required to significantly delay, scale back or discontinue one or more of our product development programs or our commercialization efforts, or other aspects of our business plan. In addition, our ability to achieve profitability or to respond to competitive pressures would be significantly limited.

We need to effectively manage the increased size and complexity of our organization to execute our business strategy.

We recently experienced significant growth in the number of our employees and the scope of our operations in connection with our commercialization of QBREXZA. Our need to manage our operations, growth and various projects effectively requires that we:

- continue to improve our operational, financial, management and regulatory compliance controls and reporting systems and procedures;
- identify, recruit, maintain, motivate and integrate additional talented employees;
- further develop our marketing, sales and distribution capabilities;
- manage our commercialization activities for QBREXZA effectively and in a cost-effective manner;
- establish and maintain relationships with development and commercialization partners;
- manage our preclinical and clinical trials effectively;

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• manage our third-party supply and manufacturing operations effectively and in a cost-effective manner, while increasing production capabilities for QBREXZA to commercial levels; and  
• manage our development efforts effectively while carrying out our contractual obligations to partners and other third parties.

In addition, historically, we have utilized and continue to utilize the services of part-time outside consultants to perform a number of tasks for us, including tasks related to preclinical and clinical testing. Our growth strategy may also entail expanding our use of consultants to implement these and other tasks going forward. We rely on consultants for certain functions of our business and will need to effectively manage these consultants to ensure that they successfully carry out their contractual obligations and meet expected deadlines. There can be no assurance that we will be able to manage our existing consultants or find other competent outside consultants, as needed, on economically reasonable terms, or at all.

To effectively manage the increased size and complexity of our organization, we may incur significant costs and our management and business development resources may be diverted. If we are unable to successfully implement the tasks necessary to effectively manage the increased size and complexity of our organization and execute our business strategy, our ability to achieve our research, development and commercialization goals may be materially adversely impacted.

If we fail to attract and retain management and other key personnel, we may be unable to continue to successfully develop our current and any future product candidates, commercialize QBREXZA or otherwise implement our business plan.

Our ability to compete in the highly competitive pharmaceuticals industry depends upon our ability to attract and retain highly qualified managerial, scientific, medical, sales and marketing and other personnel. We are highly dependent on our management and scientific personnel, including: our Chief Executive Officer and Chairman of our board of directors, Thomas G. Wiggins; our Chief Medical Officer and a member of our board of directors, Eugene A. Bauer, M.D.; our Chief Technical Operations Officer, Christopher Horan; our Chief Financial Officer, Andrew L. Guggenhime; our Chief Development Officer, Luis C. Peña; our Chief Commercial Officer, Lori Lyons-Williams; and our Chief Business and Strategy Officer, Christopher M. Griffith. The loss of the services of any of these individuals could impede, delay or prevent the successful development of our product pipeline, completion of our planned clinical trials, commercialization of our products or in-licensing or acquisition of new assets and could negatively impact our ability to successfully implement our business plan. If we lose the services of any of these individuals, we might not be able to find suitable replacements on a timely basis or at all, and our business could be harmed as a result. We do not maintain “key man” insurance policies on the lives of these individuals or the lives of any of our other employees. We employ all of our executive officers and key personnel on an at-will basis and their employment can be terminated by us or them at any time, for any reason and without notice. In order to retain valuable employees at our company, in addition to salary and cash incentives, we provide stock options and restricted stock units that vest over time. The value to employees of stock options and restricted stock units that vest over time will be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract offers from other companies. For example, following our announcement that the investigational treatment olumacostat glasaretil (formerly DRM01) for moderate-to-severe acne vulgaris did not meet the co-primary endpoints in its two Phase 3 pivotal trials (CLAREOS-1 and CLAREOS-2) in patients ages nine years and older, the value of our common stock decreased significantly, which may adversely impact our ability to attract and retain employees.

We might not be able to attract or retain qualified management and other key personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco Bay Area where we are headquartered. We could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts. Many of the other pharmaceutical companies with whom we compete for qualified personnel have greater

financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. If we are not able to attract and retain the necessary personnel to accomplish our business objectives, we may experience constraints that will harm our ability to implement our business strategy and achieve our business objectives.

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In addition, we have scientific and clinical advisors who assist us in formulating our development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

Our failure to successfully in-license, acquire, develop and market additional product candidates or approved products would impair our ability to grow our business.

We intend to in-license, acquire, develop and market additional products and product candidates. Because our internal research and development capabilities are limited, we may be dependent upon pharmaceutical companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify and select promising pharmaceutical product candidates and products, negotiate licensing or acquisition agreements with their current owners and finance these arrangements.

The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing, sales and other resources, may compete with us for the license or acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. Additionally, we may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all.

Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including preclinical or clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any approved products that we acquire will be manufactured or sold profitably or achieve market acceptance.

If we are not able to establish and maintain collaborations, we may have to alter our development and commercialization plans.

The development of product candidates and commercialization of products require substantial additional cash to fund expenses. In order to fund further development of our current and any future product candidates, we may collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. We face significant competition in seeking appropriate partners. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the partner's resources and experience, the terms and conditions of the proposed collaboration and the proposed partner's evaluation of a number of factors. Those factors may include the design or results of clinical trials; the likelihood of approval by the FDA or other regulatory authorities; the potential market for the subject product candidate; the costs and complexities of manufacturing and delivering such product candidate to patients; the potential of competing products; any uncertainty with respect to our ownership of our intellectual property; and industry and market conditions generally. The partner may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential partners. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future partners.

Collaborations typically impose detailed obligations on each party, such as those required under the Roche Agreement. If we were to breach our obligations, we may face substantial consequences, including potential termination of the collaboration, and our rights to product candidates, in which we have invested substantial time and money, would be lost.

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We may not be successful in our efforts to implement collaborations or other alternative arrangements for the development of our current or any future product candidates. When we partner with a third party for development and commercialization of a product candidate, we can expect to relinquish to the third party some of the control over the future success of that product candidate. Our collaboration partner may not devote sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization. The terms of any collaboration or other arrangement that we establish may not be favorable to us. In addition, any collaboration that we enter into may be unsuccessful in the development and commercialization of our product candidates. In some cases, we may be responsible for continuing preclinical and initial clinical development of a partnered product candidate or research program, and the payment we receive from our collaboration partner may be insufficient to cover the cost of this development.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product sales.

We face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration.

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on developing proprietary therapeutics. Numerous companies are engaged in the development, patenting, manufacturing and marketing of healthcare products competitive with those that we are developing and commercializing. We face competition from a number of sources, such as pharmaceutical companies, generic drug companies, biotechnology companies and academic and research institutions, many of which have greater financial resources, marketing capabilities, sales forces, manufacturing capabilities, research and development capabilities, clinical trial expertise, intellectual property portfolios, experience in obtaining patents and regulatory approvals for product candidates and other resources than we do. Some of the companies that offer competing products also have a broad range of other product offerings, large direct sales forces and long-term customer relationships with our target physicians, which could inhibit our market penetration efforts. In addition, QBREXZA and any of our current or future product candidates, if approved, may compete with other dermatological products, including over-the-counter (“OTC”) treatments, for a share of some patients’ discretionary budgets and for physicians’ attention within their clinical practices.

Many pharmaceutical companies currently offer products or are developing alternative product candidates and technologies, for indications similar to those targeted by our product or product candidate, including: AbbVie Inc., Allergan plc, Amgen Inc., AnaptysBio, Inc., Asana BioSciences, LLC, Aslan Pharmaceuticals Pte Ltd., Brickell Biotech, Inc., Dermavant Sciences Ltd. (a subsidiary of Roivant Sciences), Chugai Pharmaceutical Co., DS Biopharma Limited, Eirion Therapeutics, Inc., Eli Lilly and Company, Galapagos NV, Galderma S.A., GlaxoSmithKline LLC, Glenmark Pharmaceuticals Limited, LEO Pharma A/S, Maruho Co., Ltd., MedImmune, LLC (a wholly-owned subsidiary of AstraZeneca plc), Menlo Therapeutics Inc., Miramar Labs, Inc., MorphoSys AG, Mylan Inc., Novartis AG, Pfizer Inc., Ltd., Regeneron Pharmaceuticals, Inc., Sandoz International GmbH (a division of Novartis), Sanofi-Aventis Groupe S.A., Teva Pharmaceutical Industries Ltd., Ulthera, Inc. (a subsidiary of Merz Pharma GmbH & Co. KGaA), Valeant Pharmaceuticals International, Inc., Vanda Pharmaceuticals Inc. and XBiotech Inc.



The markets for dermatological therapies are competitive and are characterized by significant technological development and new product introduction. We anticipate that QBREXZA and any of our current or future product candidates, if approved, will face significant competition from other approved therapies as well as unregulated, unapproved and off-label treatments. QBREXZA and any of our current or future product candidates, if approved, would present novel therapeutic approaches for the approved indications and would have to compete with existing therapies, some of which are widely known and accepted by physicians and patients. To compete successfully in this market, we will have to demonstrate that the relative cost, safety and efficacy of our approved product provide an attractive alternative to existing and other new therapies. The competition we face could lead to reduced market

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share for QBREXZA and any of our current or future product candidates that are approved and contribute to downward pressure on the pricing of our products, which could harm our business, financial condition, operating results and prospects.

Due to less stringent regulatory requirements in certain foreign countries, there are many more dermatological products and procedures available for use in those international markets than are approved for use in the United States. In certain international markets, there are also fewer limitations on the claims that our competitors can make about the effectiveness of their products and the manner in which they can market their products. As a result, we expect to face more competition in these markets than in the United States.

We expect to face generic competition and may face competition from biosimilars, which could adversely affect our business, financial condition, operating results and prospects.

Upon the expiration or loss of any patent protection for QBREXZA and our current and any future product candidates that are approved, or upon the “at-risk” launch by a generic competitor of a generic version of QBREXZA or our current and any future product candidates that are approved, which may be sold at significantly lower prices than our approved product candidates, we could lose a significant portion of sales of that product in a short period of time, which would adversely affect our business, financial condition, operating results and prospects. In particular, QBREXZA faces competition from currently marketed generic oral and compounded topical anticholinergic agents. In addition, we may be subject to additional competition from third parties pursuing topical formulations of other anticholinergic agents for hyperhidrosis.

We may also face competition from biosimilars. In the United States, the Biologics Price Competition and Innovation Act of 2009 (“BPCIA”) created an abbreviated approval pathway for biological products that are demonstrated to be “highly similar,” or “biosimilar,” to or “interchangeable” with an FDA-approved biological product. This pathway allows competitors to reference the FDA’s prior determinations regarding innovative biological products and to obtain approval of a biosimilar application 12 years after the time of approval of the innovative biological product. The 12-year exclusivity period runs from the initial approval of the innovator product and not from approval of a new indication. In addition, the 12-year exclusivity period does not prevent another company from developing a product that is highly similar to the innovative product, generating all the data necessary for a full BLA and seeking approval. Exclusivity only assures that another company cannot rely on the FDA’s prior determinations in approving a BLA for an innovator’s biological product to support the biosimilar product’s approval. Further, under the FDA’s current interpretation, it is possible that a biosimilar applicant could obtain approval for one or more of the indications approved for the innovator product by extrapolating clinical data from one indication to support approval for the other indications. We cannot predict to what extent the entry of biosimilars or other competing products will impact our business, financial condition, operating results and prospects.

Manufacturing and supply of the drug substance and other substances and materials used in product and product candidate is a complex and technically challenging undertaking, and there is potential for failure at many points in the manufacturing, testing, quality assurance and distribution supply chain, as well as the potential for latent defects after products have been manufactured and distributed.

Manufacturing and supply of drug substance, other substances and materials and finished drug products is technically challenging. Changes beyond our direct control can impact the quality, volume, price and successful delivery of our product and current or future product candidates and can impede, delay, limit or prevent the successful commercialization of QBREXZA and development of our current or future product candidates. Mistakes and mishandling are not uncommon and can affect successful production and supply. Some of these risks include:

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failure of our manufacturers to follow cGMP requirements or mishandling of product while in production or in preparation for transit;  
• inability of our contract suppliers and manufacturers to efficiently and cost-effectively increase and maintain high yields and batch quality, consistency and stability;  
• inability of our suppliers and manufacturers to meet our production demands due to issues related to their reliance on sole-source suppliers and manufacturers;

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• difficulty in establishing optimal production, storage, packaging and shipment methods and processes;  
• challenges in designing effective drug delivery devices and techniques;  
• transportation and import/export risk, particularly given the global nature of our supply chain;  
• delays in analytical results or failure of analytical techniques that we depend on for quality control and release of product;  
• natural disasters, labor disputes, financial distress, lack of raw material supply, issues with facilities and equipment or other forms of disruption to the business operations of our contract manufacturers and suppliers; and  
• latent defects that may become apparent after product has been released and which may result in recall and destruction of product.

Any of these factors could result in delays or higher costs in connection with our clinical trials, regulatory submissions, required approvals or commercialization of our product, which could harm our business, financial condition, operating results and prospects.

We may choose to discontinue the development of our current or any future product candidates or commercialization of any approved products, which would reduce or eliminate our potential return on investment for those product candidates or product.

At any time, we may decide to discontinue the development of our current or any future product candidates or commercialization of our approved products for a variety of reasons, such as the appearance of new technologies that make our product obsolete, competition from a competing product, changes in or failure to comply with applicable regulatory requirements, the discovery of unforeseen side effects after the approved product has been marketed or the occurrence of adverse events at a rate or severity level that is greater than experienced in our clinical trials. If we terminate a program in which we have invested significant resources, we will not receive any return on our investment and we will have missed the opportunity to have allocated those resources to potentially more productive uses.

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

The manufacturing activities of our third-party suppliers and manufacturers involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our product, product candidates and other hazardous compounds. 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 suppliers' or manufacturers' facilities pending use and disposal. We and our suppliers and manufacturers cannot completely eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, injury to our service providers and others and 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 suppliers and 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. We do not currently carry biological or hazardous waste insurance coverage.

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Our employees, independent contractors, principal investigators, consultants, vendors, CROs, distributors, prescribers and any partners with which we may collaborate may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our business.

We are exposed to the risk that our employees, independent contractors, principal investigators, consultants, vendors, CROs, distributors, prescribers and any partners with which we may collaborate may engage in fraudulent or other illegal activity. Misconduct by these persons could include intentional, reckless or negligent conduct or unauthorized activity that violates: laws or regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA or foreign regulatory authorities; manufacturing standards; federal, state and foreign healthcare fraud and abuse laws and data privacy; or laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of business activities, including research, manufacturing, distribution, pricing, discounting, marketing and promotion, sales commissions, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials, or illegal misappropriation of drug product, which could result in regulatory sanctions or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations, and serious harm to our reputation. In addition, federal procurement laws impose substantial penalties for misconduct in connection with government contracts and require certain contractors to maintain a code of business ethics and conduct. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our operating results.

We intend to in-license and acquire product candidates or engage in other strategic transactions, which could impact our liquidity, increase our expenses and present significant distractions to our management.

Our strategy is to in-license and acquire product candidates or engage in other strategic transactions. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near- and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions entail numerous potential operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention in order to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;
- substantial acquisition and integration costs;
- write-downs of assets or impairment charges;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers, partners or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain our key employees or those of any acquired businesses.

Accordingly, there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, and any transaction that we do complete could harm our business, financial condition,

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operating results and prospects. We have no current plan, commitment or obligation to enter into any transaction described above.

Our future operating results are difficult to predict and may fluctuate significantly. Our gross-to-net estimates related to revenue recognition from product sales are difficult to estimate and if our estimates differ significantly from actual product sales, we will be required to record an adjustment in a subsequent period. If our operating results fall below expectations, our stock price may be adversely impacted.

Our operations to date have been primarily limited to researching and developing our product candidates, undertaking preclinical studies and clinical trials of our product candidates and, more recently, preparing for the commercial launch of QBREXZA. QBREXZA, our only product approved for commercialization, became available in pharmacies nationwide on October 1, 2018. Our revenue and profitability will depend in large part on the successful commercialization of QBREXZA. Our future operating results are difficult to predict and may fluctuate significantly from period to period due to many factors, such as revenue from product sales, expenditures and payments relating to collaboration and license agreements and stock-based compensation expense.

Our gross-to-net estimates related to revenue recognition from product sales are difficult to estimate as they are based on multiple assumptions which may prove to be incorrect. For example, we contract with certain third-party payers for the payment of rebates with respect to the utilization of QBREXZA and rebates to these payers are based on contractual percentages applied to the amount of QBREXZA prescribed to patients who are covered by the plan or the organization with which the third-party payer contracts. We have also implemented a savings card program to provide assistance to eligible patients with out-of-pocket costs, such as deductibles, co-insurance and co-payments, for the patient's usage of QBREXZA. Reductions to product sales for the savings card program are estimated based on actual and expected program utilization. We recognize product sales at the transaction price, net of estimates of variable consideration, including commercial rebates, discounts related to a patient savings card program, distribution fees, trade discounts, government rebates and chargebacks and product returns. Our estimates of variable consideration are based on assumptions relating to, among other things, the mix of patients who purchase QBREXZA who are fully insured, underinsured and uninsured and the utilization of our savings card program, rebates, discounts and other pricing concessions and fees. If our gross-to-net estimates differ significantly from actual product sales, we will be required to record an adjustment in a subsequent period to reported product sales and earnings.

From time to time, we may enter into collaboration agreements and license agreements with other companies that include development funding and significant upfront and milestone expenditures and payments. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next.

In addition, we measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award as determined by our board of directors, and recognize the cost as an expense over the employee's requisite service period. As the variables that we use as a basis for valuing these awards change over time, including our underlying stock price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly.

Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the following:

- delays in the commencement, patient enrollment and the timing of clinical testing for our current and any future product candidates;
- the timing and success or failure of clinical trials for our current and any future product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among

our competitors or partners;

any delays in regulatory review and approval of current and any future product candidates in clinical development;  
the timing and cost of, and level of investment in, research and development activities relating to our current and any future product candidates, which may change from time to time;

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the cost of manufacturing our current and any future product candidates, which may vary depending on FDA guidelines and requirements, and the quantity of production;

our ability to obtain additional funding to develop our current and any future product candidates;

expenditures that we will or may incur to acquire or develop additional product candidates and technologies;

the level of demand for our current and any future product candidates, should they receive approval, which may vary significantly;

potential side effects of our current and any future product candidates that could delay or prevent commercialization or cause an approved drug to be taken off the market;

the availability of formulary coverage and adequate reimbursement from private third-party payers for our current and any future product candidates that may be approved;

gross-to-net deductions, including rebates, discount, other pricing concessions and fees that we may provide to integrated delivery networks, group purchasing organizations, other purchasers and pharmacy benefits managers and other third-party payers;

the mix of fully insured, underinsured and uninsured patients who purchase QBREXZA and the utilization of our savings card program;

our dependency on third-party manufacturers to supply or manufacture our current and any future product candidates;

our ability to maintain an effective sales and our marketing and distribution infrastructure that supports our commercial growth;

market acceptance of our current and any future products, if approved, and our ability to forecast demand for those products;

- our ability to receive regulatory approval and commercialize our current and any future product candidates;

our ability to establish and maintain collaborations, licensing or other arrangements;

our ability and third parties' abilities to protect intellectual property rights;

costs related to and outcomes of potential litigation or other disputes;

our ability to adequately support future growth;

our ability to attract and retain key personnel to manage our business effectively;

potential liabilities associated with hazardous materials;

our ability to maintain adequate insurance policies; and

future accounting pronouncements or changes in our accounting policies.

Our operating results and liquidity needs could be negatively affected by market fluctuations and economic downturn.

Our operating results and liquidity could be negatively affected by economic conditions generally, both in the United States and elsewhere around the world. The market for discretionary medical products and procedures may be particularly vulnerable to unfavorable economic conditions. Some patients may consider QBREXZA as discretionary, and if full reimbursement for the product is not available, demand for the product may be tied to the discretionary spending levels of our targeted patient populations. Domestic and international equity and debt markets have experienced and may continue to experience heightened volatility and turmoil based on domestic and international economic conditions and concerns. In the event these economic conditions and concerns continue or worsen and the markets continue to remain volatile, our operating results and liquidity could be adversely affected

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by those factors in many ways, including weakening demand for QBREXZA, making it more difficult for us to raise funds if necessary, and our stock price may decline.

Our ability to utilize our net operating loss (“NOL”) carryforwards and research and development income tax credit carryforwards may be limited.

As of December 31, 2018, we had NOL carryforwards available to reduce future taxable income, if any, for federal, California and Canadian income tax purposes. If not utilized, the federal and California NOL carryforwards will begin expiring during the year ending December 31, 2030 and the Canadian NOL carryforwards will begin expiring during the year ending December 31, 2028. Under Section 382 of the Internal Revenue Code of 1986, as amended (the “Code”), if a corporation undergoes an “ownership change,” generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation’s ability to use its pre-change NOL carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We have experienced at least one ownership change since inception and our utilization of NOL carryforwards will therefore be subject to annual limitation. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

We may be adversely affected by natural disasters and other catastrophic events, and by man-made problems such as terrorism, that could disrupt our business operations and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters are located in Menlo Park, California, near major earthquake and fire zones. If a 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 enterprise financial systems, manufacturing resource planning or 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. Our contract manufacturers’ and suppliers’ facilities are located in multiple locations, where other natural disasters or similar events, such as blizzards, tornadoes, fires, explosions or large-scale accidents or power outages, could severely disrupt our operations and have a material adverse effect on our business, financial condition, operating results and prospects. In addition, acts of terrorism and other geo-political unrest could cause disruptions in our business or the businesses of our partners, manufacturers or the economy as a whole. All of the aforementioned risks may be further increased if we do not implement a disaster recovery plan or our partners’ or manufacturers’ disaster recovery plans prove to be inadequate. To the extent that any of the above should result in delays in the regulatory approval, manufacture, distribution or commercialization of our product or product candidates, our business, financial condition, operating results and prospects would suffer.

Our business and operations would suffer in the event of failure, invasion, corruption, destruction or interruption of our or our partners’ critical information technology systems or infrastructure.

Despite the implementation of security measures, our information technology systems and infrastructure, and those of our current and any future partners, contractors and consultants, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. The ever-increasing use and evolution of technology, including cloud-based computing, creates opportunities for the unintentional dissemination or intentional destruction of confidential information stored in our systems or in non-encrypted portable media or storage devices. We could also experience a business interruption, intentional theft of confidential information, or reputational damage from espionage attacks, malware or other cyber-attacks, which may compromise our system infrastructure or lead to data leakage, either internally or at our third-party providers. While

we have not experienced any such material 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 manufacturing activities, development programs and our business operations. For example, the loss of manufacturing records or clinical trial data from completed, ongoing or future clinical trials 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

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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 current and any future product candidates and commercialization of our product could be delayed.

Risks Related to Our Industry

Healthcare reform measures could hinder or prevent the commercial success of our product and product candidates.

In the United States, 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 revenue and profitability and the future revenue and profitability of any partner with which we may collaborate. Federal and state lawmakers regularly propose and, at times, enact legislation that results in significant changes to the healthcare system, some of which are intended to contain or reduce the costs of medical products and services. For example, in March 2010, former President Obama signed one of the most significant healthcare reform measures in decades, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, “Affordable Care Act”). It contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse measures, all of which have impacted and are expected to continue to impact existing government healthcare programs and result in the development of new programs. The Affordable Care Act, among other things, (1) increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to certain individuals enrolled in Medicaid managed care organizations, (2) established annual fees on manufacturers of certain branded prescription drugs and (3) enacted 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.

The current presidential administration and certain members of the majority of the U.S. Congress have sought to repeal all or part of the Affordable Care Act and implement a replacement program. For example, the so-called “individual mandate” was repealed as part of tax reform legislation adopted in December 2017, such that the shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Code will be eliminated beginning in 2019. In addition, litigation may prevent some or all of the Affordable Care Act legislation from taking effect. For example, on December 14, 2018, the U.S. District Court for the Northern District of Texas held that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the tax reform legislation, the remaining provisions of the Affordable Care Act are invalid as well. The impact of this ruling is stayed as it is appealed to the Fifth Circuit Court of Appeals. While the ruling will have no immediate effect, it is unclear how this decision, and subsequent appeals, if any, will impact the law. In 2019 and beyond, we may face additional uncertainties as a result of likely federal and administrative efforts to repeal, substantially modify or invalidate some or all of the provisions of the Affordable Care Act. There is no assurance that the Affordable Care Act, as amended in the future, will not adversely affect our business and financial results. Additionally, in October 2018, the U.S. President has proposed to lower Medicare Part B drug prices, in addition to contemplating other measures to lower prescription drug prices. While this proposal has not yet been enacted, we expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our approved product or additional pricing pressures.

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We may also be subject to healthcare laws, regulation and enforcement and our failure to comply with those laws could adversely affect our business, operations and financial condition.

Certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights, among other topics, are and will be applicable to our business. We are subject to regulation by both the federal government and the states in which we or our partners conduct our business. The healthcare laws and regulations that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, any person or entity from knowingly and willfully offering, soliciting, receiving or providing any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce either the referral of an individual or in return for the purchase, lease, or order of any good, facility item or service, for which payment may be made, in whole or in part, under federal healthcare programs such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, including, for example, the federal civil False Claims Act, which impose criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payer (e.g., public or private), 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 by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations, which impose obligations on covered entities, including certain healthcare providers, health plans, and healthcare clearinghouses, as well as their respective business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal physician sunshine requirements under the Affordable Care Act, which require certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value provided to physicians and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members;
- federal and state laws requiring pricing transparency or limiting price increases, which are in existence today or are anticipated to be in existence in the near future, may limit the ability to raise prices, require disclosure of price increases or require disclosure of the wholesale acquisition cost of pharmaceutical products to governmental agencies and consumers; and

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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 payer, 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 provided 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 healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent healthcare reform legislation has strengthened these laws. For example, the Affordable Care Act, among other things, amended the intent requirement of the federal Anti-Kickback Statute and certain criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act codified case law 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 civil False Claims Act.

Achieving and sustaining compliance with these laws may prove costly. In addition, 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 or regulations that apply to us, we may be subject to penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, the exclusion from participation in federal and state healthcare programs, individual imprisonment or the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results.

### Risks Related to Our Intellectual Property

We may not be able to obtain or enforce patent rights or other intellectual property rights that cover our product, product candidates and technologies that are of sufficient breadth to prevent third parties from competing against us.

Our success will depend in part on our ability to obtain and maintain patent protection in both the United States and other countries, to preserve our trade secrets and to prevent third parties from infringing upon our proprietary rights. Our ability to protect against unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents.

Our patent portfolio includes patents and patent applications in the United States and foreign jurisdictions where we believe there is a market opportunity for our product and product candidates. The covered technology and the scope of coverage vary from country to country. For those countries where we do not have granted patents, we may not have any ability to prevent the unauthorized use of our technologies. Any patents that we may obtain may be narrow in scope and thus easily circumvented by competitors. Further, in countries where we do not have granted patents, third parties may be able to make, use or sell products identical to or substantially similar to, our product or product candidates.

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The patent application process, also known as patent prosecution, is expensive and time-consuming, and we and our current or future licensors and licensees may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our current licensors or licensees, or any future licensors or licensees, will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, these and any of our patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If our current licensors or licensees, or any future licensors or licensees, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised and we might not be able to prevent third parties from making, using and selling competing products. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business, financial condition and operating results.

Due to legal standards relating to patentability, validity, enforceability and claim scope of patents covering pharmaceutical inventions, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions. Accordingly, rights under any existing patents or any patents we might obtain or license may not cover our product or product candidates, or may not provide us with sufficient protection for our product or product candidates to afford a commercial advantage against competitive products or processes, including those from branded and generic pharmaceutical companies. In addition, we cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us. Even if patents have issued or will issue, we cannot guarantee that the claims of these patents are or will be held valid or enforceable if challenged in post-grant proceedings or by the courts or will provide us with any significant protection against competitive products or otherwise be commercially valuable to us.

Competitors in the field of dermatologic therapeutics have created a substantial amount of prior art, including scientific publications, patents and patent applications. Our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Although we believe that our technology includes certain inventions that are unique and not duplicative of any prior art, we do not have outstanding issued patents covering all of the recent developments in our technology and we are unsure of the patent protection that we will be successful in obtaining, if any. Even if the patents do successfully issue, third parties may design around or challenge the validity, enforceability or scope of such issued patents or any other issued patents we own or license, which may result in such patents being narrowed, invalidated or held unenforceable. In particular, due to the extensive prior art relating to anticholinergic agents to control hyperhidrosis and because glycopyrronium tosylate is a form of a generic anticholinergic agent, the patent protection available for glycopyrronium tosylate may not prevent competitors from developing and commercializing similar products. If the breadth or strength of protection provided by the patents we hold or pursue with respect to our product or product candidates is challenged, it could dissuade companies from collaborating with us to develop, or threaten our ability to commercialize, our product or product candidates.

The laws of some foreign jurisdictions do not provide intellectual property rights to the same extent as in the United States and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property in foreign jurisdictions, our business prospects could be substantially harmed.

The degree of future protection of our proprietary rights is uncertain. Patent protection may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we might not have been the first to invent or the first to file the inventions covered by each of our pending patent applications and issued patents;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;

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- the patents of others may have an adverse effect on our business;
- any patents we obtain or our licensors' issued patents may not encompass commercially viable products, may not provide us with any competitive advantages or may be challenged by third parties;
- any patents we obtain or our in-licensed issued patents may not be valid or enforceable; and
- we may not develop additional proprietary technologies that are patentable or provide us with a competitive advantage.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our product and product candidates, we may be open to competition from generic versions of our product and product candidates. Further, the extensive period of time between patent filing and regulatory approval for a product or product candidate limits the time during which we can market a product under patent protection, which may particularly affect the profitability early-stage product candidates. The issued U.S. patents relating to glycopyrronium tosylate and lebrikizumab will expire between 2020 and 2037.

Proprietary trade secrets and unpatented know-how are also very important to our business. Although we have taken steps to protect our trade secrets and unpatented know-how by entering into confidentiality agreements with third parties, and intellectual property protection agreements with certain employees, consultants and advisors, third parties may still obtain this information or we may be unable to protect our rights. We also have limited control over the protection of trade secrets used by our suppliers, manufacturers and other third parties. There can be no assurance that binding agreements will not be breached, that we would have adequate remedies for any breach or that our trade secrets and unpatented know-how will not otherwise become known or be independently discovered by our competitors. If trade secrets are independently discovered, we would not be able to prevent their use. Enforcing a claim that a third party illegally obtained and is using our trade secrets or unpatented know-how is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secret information.

Changes in patent laws or the interpretations of patent laws could diminish the value of patents in general, thereby impairing our ability to protect our product and product candidates.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. The United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Further, recent U.S. Supreme Court rulings have either narrowed the scope of patent protection available in certain circumstances or weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the scope and value of patents, once obtained.

For our U.S. patent applications containing a priority claim after March 16, 2013, there is a greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act, also known as the America Invents Act ("AIA") was signed into law. The AIA includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have an adverse effect on our business. An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the U.S. Patent and Trademark Office ("USPTO") after that date but before us could therefore be awarded a patent covering an invention of ours even if

we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application.

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Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and provide opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by t