

## Revance Therapeutics, Inc.

### Initiating Coverage With Outperform Rating and \$35 Price Target

Revance is developing two highly differentiated next-generation botulinum toxin products, RT001 and RT002. RT001 is the more controversial of the two; however, given the potential for the topical formulation, we believe it represents a significant risk/reward from current levels. We note, however, that the company's ongoing delay in the initiation of the RT001 Phase III program is frustrating, although proof of concept in hyperhidrosis (HH) will come in early 2015, and the indication does not hold the same regulatory risks that will come with the lateral canthal lines indication.

Aside from the controversy over RT001 endpoints, we would argue that the company's current valuation is attractive based solely on the potential for RT002, the company's long-duration injectable botulinum toxin. RT002 also should not be exposed to the FDA disagreements over LCL endpoints and could be a blockbuster product in therapeutic indications. Moreover, the company plans to initiate a direct comparator study against Botox in glabellar lines by the end of this year, which would be a powerful study if a significant difference in duration of effect is shown in the same patient population. Interim results of this study are expected in late 2015 and should be a major catalyst for shares.

Although the recent news flow from Revance has been frustrating to shareholders, giving even 25% probability for success of RT001 and 40% probability for success of RT002, we derive a \$35 net present value for Revance's pipeline. Although the stock has sold off in recent months, we believe the company has several major catalysts in 2015 and shares hold a strong risk/reward profile with the company's enterprise value of \$200 million, which is the lowest among comparable specialty pharmaceutical companies with late-stage assets. Ultimately from current levels, we believe proof of concept in either RT001 or RT002 would lead to significant upside, and we are initiating coverage with an Outperform rating and Aggressive Growth company profile.

Risks to investing in Revance include clinical, regulatory, and commercial risks given the development stage of the company. Risks unique to Revance include the recently issued FDA guidance regarding upper-face aesthetic procedures and the manufacturing transfer process of its botulinum toxin formulation.

*Revance Therapeutics, Inc. is a clinical-stage pharmaceutical company focused on the development, manufacturing, and commercialization of novel botulinum toxin products using its proprietary TransMTS technology.*

December 9, 2014

**Basic Report** (14-156)

Stock Rating: **Outperform**  
Company Profile: **Aggressive Growth**  
Price Target: \$35

Symbol: RVNC (NASDAQ)  
Price: \$17.42 (52-Wk.: \$16-\$40)  
Market Value (mil.): \$413  
Fiscal Year End: December

Estimates	2013A	2014E	2015E
EPS FY	-\$2.69	-\$3.16	-\$2.49
EBITDA (mil.)	-\$32	-\$44	-\$52

#### Trading Data

Shares Outstanding (mil.)	23.72
Float (mil.)	15.76
Average Daily Volume	218,105

#### Financial Data

Long-Term Debt/Total Capital	NM
Book Value Per Share	NM
Enterprise Value (mil.)	236.9
EBITDA (mil.)	NM
Enterprise Value/EBITDA	NM

**Tim Lugo**  
+1 415 248 2870  
tlugo@williamblair.com

**Raju Prasad, Ph.D.**  
+1 312 364 8469  
rprasad@williamblair.com

Please refer to important disclosures on pages 43 and 44. Analyst certification is on page 43. William Blair does and seeks to do business with companies covered in its research reports. As a result, investors should be aware that the firm may have a conflict of interest that could affect the objectivity of this report. Investors should consider this report as a single factor in making an investment decision.

## Contents

<b>Company Overview</b>	3
<b>Key Risks</b>	4
<b>Deep Dive in Efficacy Assessment in Aesthetics</b>	5
<b>FDA Draft Guidance Continues Endpoint Debate</b>	7
<b>Overview of Botulinum Toxin Type A</b>	9
<b>Overview of TransMTS Peptide Technology</b>	9
<b>Pipeline Overview</b>	12
<b>RT001: Delays Have Been Frustrating, but Opportunity Keeps Development Moving Forward</b>	14
<b>RT002: Long-Acting Injectable Could Be Blockbuster in Therapeutic Indications</b>	26
<b>Competition</b>	31
<b>Management Team</b>	34
<b>Financial Overview</b>	35
<b>Valuation and Stock Thoughts</b>	37
<b>Conclusion</b>	39

## Company Overview

Revanche Therapeutics, based in Newark, California, is a development-stage biopharmaceutical company that uses its proprietary TransMTS peptide technology for delivery of botulinum toxin both as a topical application, in RT001, and as an injectable with a longer duration of effect, in RT002. The company has shown safety and efficacy of its lead candidate, RT001 for the indication of lateral canthal lines (LCL, commonly known as “crow’s feet”), in multiple Phase II studies in more than 1,400 subjects to date. Yet the development of RT001 has not been linear and without controversy.

The key to our Outperform rating is that we believe proof-of-concept data from RT002, the company’s long-duration injectable botulinum toxin, may suggest a best-in-class product for the therapeutic setting with an aggressive head-to-head trial to be initiated by the end of 2014, which will have an interim readout in 2015. While the proof-of-concept study for RT002 will be in glabellar lines (commonly called “frown lines”), we believe that the product, with a potentially best-in-class duration of effect, may be destined as a product in the movement disorder setting and select indications. We also like that RT002 is not exposed to the FDA disagreements over upper-facial endpoints and the “at rest” versus “at maximal smile” endpoints.

RT002 has been shown to have an effect up to 7.3 months after initial injection in the aesthetic indication of smoothing glabellar lines, which would reduce the frequency of injections by roughly one-half from the average treatment with Botox/Dysport/Xeomin, the three products currently approved for this indication (duration of about three to four months). Because the majority of people who use cosmetic botulinum toxin injections are repeat users, we believe that, if approved for the indication of glabellar lines, RT002 could be a blockbuster therapy.

Development of RT001 has been longer than the company had anticipated. Multiple dosing strategies led to a significant number of Phase II studies; the company has also already conducted a failed Phase III study in LCL as a result of issues with a formulation change between Phase II and the failed Phase III. The company has since addressed these concerns with a two-year study showing commercial-level stability of its old formulation (the formulation used in its positive Phase IIb clinical trial data) and conducted a Phase II study after reverting to the initial formula (a fourth Phase II study for RT001). Recently, after examining 32 of 43 patients in an open-label study of RT001 using its own manufacturing facilities, the company saw promising results; however, the two-point response rates were lower than its previous studies, leading to the need to delay its Phase III program. Depending on another open-label trial using the company’s manufacturing, we expect an update regarding the initiation of its Phase III program for RT001 in LCL in the first quarter of 2015.

In addition to the recent clinical setback, shares were weak after the release of FDA draft guidance on endpoints within development of aesthetic products, such as RT001. In particular, the guidance document notes that upper-facial procedures were to be measured at maximal muscle contraction; for LCL, this would be a measurement of efficacy at maximal smile versus at rest, which is the primary endpoint included in the current RT001 Phase III program. After discussions with consultants, we agree with the company’s view that the FDA draft guidance should be viewed as a summary of data to date and a document that is meant to provoke discussion in the industry after Revance prevailed in its dispute resolution process with the FDA over the same issue in 2013. In addition, a public response from three leading physicians in the space has called into question the endpoints of assessment at maximal contraction and a required two-point benefit, primarily based on the desire to distinguish between an objectively measurable clinical trial endpoint and a real-world scenario in which a “more natural look” is the key to efficacy. We believe that data to be produced from Revance’s Phase III LCL studies should provide the supportive data necessary to argue for the at-rest endpoint. And while consultants we have spoken with suggest that RT001 is likely a product with

milder efficacy than the injectable products, we believe there will be a role for a topically applied product for LCL and likely other indications in patients who would prefer a more natural (and likely milder) aesthetic outcome without the need for injections.

Exhibit 1 details the timeline of major events over the next three years as the company advances its clinical programs for both RT001 and RT002.

**Exhibit 1**  
**Revance Therapeutics, Inc.**  
**Timeline and Events**

Date	Product	Event	Description/Comments
<b>2014</b>			
4Q 2014	RT002	Clinical	Initiate Phase II comparator trial vs. Botox in glabellar lines (n=250)
<b>2015</b>			
1Q15	RT001	Clinical	Initiate second Phase II using scale-up material
1Q15	RT001	Clinical	Initiate Phase II study in hyperhidrosis
2015	RT001	Clinical	Initiate 1st U.S. Phase III in crow's feet lines (n=170)
2015	RT001	Clinical	Interim data from open-label safety trial (n=1800)
2015	RT001	Clinical	Report data from EU Phase III in crow's feet lines
2015	RT001	Clinical	Report Phase II data in hyperhidrosis
2015	RT002	Clinical	Report interim Phase II data from comparator trial in glabellar lines
<b>2016</b>			
2016	RT001	Clinical	Report U.S. long-term safety data

Sources: Company reports and William Blair & Company, L.L.C. estimates

## Key Risks

Revance faces several risks to the development and commercialization of both RT001 and RT002. Risks include those that are common among the company's development-stage peers: clinical risk, manufacturing risk, and regulatory risk.

**Both pipeline candidates, RT001 and RT002, face clinical risks.** The development of compounds through clinical trials has inherent risks. The company experienced a clinical setback in a prior failed Phase III trial that exhibited placebo-like efficacy. The company was able to determine that the failed results were because of new additives in the formulation and has reverted to the same formulation used in the successful Phase II program. Another Phase II study also had some trial mistakes that were identified and corrected in a subsequent cohort. Its latest confirmatory Phase II trial using its own manufacturing facility of RT001 yielded encouraging but inconsistent results, and significant clinical risk remains.

***The manufacturing of botulinum toxin type A is a complicated process with inherent risks.*** The company has one manufacturing facility to support both RT001 and RT002. While we believe that controlling manufacturing is a significant strategic asset, the process is relatively complex versus small-molecule drug development. While Revance is scaling manufacturing internally, there is always a risk when young companies bring complicated manufacturing processes to scale. We are seeing this play out currently in the Phase II open-label studies that are ongoing for RT001. It should be noted that botulinum toxin type A is a known toxin, and regulatory scrutiny will likely be strict.

***Given the recent FDA guidance, regulatory risk remains, but we believe that RT002 is shielded from the controversy and holds less regulatory risk.*** As was reflected in the recent share price weakness following the release of FDA draft guidance on the development of aesthetic products, the FDA may again raise issues with the at-rest endpoint used in the development of RT001 for LCL. While Revance prevailed in a prior dispute resolution with the division, the recent guidance document suggests that we likely have not seen the last of this issue.

***The company is entering an established market with a leader that has significant market share, so there is competitive risk and the potential for lower-than-expected market penetration.*** RT001 and RT002 are both botulinum toxin type A products, of which Botox is the market leader, with a 76% share; the second product, Dysport, has about 15% share. While we view both RT001 and RT002 as differentiated products, when brought to market, they will likely compete with entrenched brands for several indications, such as LCL, glabellar lines, and movement disorders.

## Deep Dive in Efficacy Assessment in Aesthetics

As the controversy over endpoints in development of products for facial aesthetics highlights, it is important to understand the endpoints and measurements used to assess efficacy in this category of products. As we look over several product categories in the aesthetic space, the endpoints often vary to some degree in the same product category, and the current at rest versus at maximal smile debate likely is a continuation of this heterogeneity in clinical endpoints.

According to studies conducted by the SMILE Study Group, clinical scales using four-point scores of 0 (none) to 3 (severe) for LCL both at rest and maximum smile show good reproducibility and are recommended for use in clinical trials (Hund et al. *Dermatol Surg*, 2006). Particularly, the SMILE Study involved an assessment of 49 photographs at rest and 48 at maximum smile by the same group of investigators on two consecutive days (N=9 on day one, N=8 on day two), wherein a weighted measurement was used for the level of agreement in observations between 0 (no agreement) and 1 (absolute agreement). A value of <0.20 was considered a poor agreement, 0.21 to 0.40 fair, 0.41 to 0.60 moderate, 0.61 to 0.80 good, and 0.81 to 1.00 very good (Altman DG, *Practical Statistics for Medical Research*, 1998). In the study, weighted kappa varied between 0.63 and 0.91 at rest, and at maximum smile the weighted kappa varied between 0.71 and 0.85. The study concluded that, with careful training to ensure consistency, a four-point scale is an appropriate, reproducible measurement mechanism for LCL.

Companies with FDA-approved products in the past have used a combination of physician assessment and subject assessment for efficacy, which makes the overall assessment and comparability between clinical trials difficult. Botox, the market leader by Allergan, used both an investigator and subject four-point facial wrinkle scale (FWS) as the primary endpoint to assess the severity of the patient's LCL at both rest and maximum smile in Phase III trials. A responder was defined as a participant with a  $\geq 2$ -grade improvement from baseline. Secondary endpoints in these clinical trials consisted of the percentage of participants achieving a grade of none/mild on FWS at maximum smile,  $\geq 1$ -grade improvement on FWS at maximum smile, and  $\geq 1$ -grade improvement on FWS at rest. For subject assessment, Allergan used the Facial Line Outcomes Questionnaire (FLO) based on

a 0-10 subjective scale; in particular, items 2 (defined as participants with  $\geq 2$ -grade improvement in the question, “When I look in the mirror, my facial lines make me look older than I want to look.”), 5 (defined as participants with a  $\geq 2$ -grade improvement in the question, “My facial lines make me look less attractive than I want to look.”), and 8 (defined as participants with a  $\geq 3$ -grade improvement in the question, “My facial lines make me look tired.”) were used to assess psychological impact. In a study presented at the American Society of Dermatologic Surgery (ASDS) annual meeting in 2013, these three items in FLO were significantly greater in patients with moderate to severe LCL treated with Botox compared with placebo (item 2: 70% versus 28%; item 5: 66.8% versus 22.8%; and item 8: 55.8% versus 16.3%;  $p < 0.001$  for all comparisons).

The two main Botox competitors, Dysport and Xeomin, were approved for use in glabellar lines in 2009 and 2011, respectively. Clinical trials with all three compounds for use in glabellar lines established none or mild lines with at least two-grade improvement from baseline at maximum frown for the combined investigator and subject assessments (composite score) at day 30 as the primary endpoint. Furthermore, both Dysport and Xeomin used a four-point scale to assess efficacy at maximum frown for glabellar lines.

Revance’s clinical studies to date have used both an investigator global assessment (IGA) and a patient assessment for LCL at rest and at maximum smile, with the at-rest composite score used as the primary endpoint in the Phase III clinical program and with the scores in maximum contraction used as secondary endpoints (i.e., they will not be reported in the top-line readouts). Exhibit 2 shows the definition of the scale for Revance’s IGA assessment, which uses a five-point scale (with the other products graded on four-point scales for the efficacy reported on their labels for both LCL and glabellar lines).

Exhibit 2  
Revance Therapeutics, Inc.  
Revance Facial Wrinkle Scale

Grade of Nasolabial Fold	Description
0 (Absent)	No visible wrinkles
1 (Minimal)	Minimal wrinkles, within 1.5-cm radius of the lateral canthus and may be minimally etched
2 (Mild)	Shallow wrinkles, extending between 1.5- and 2.5-cm radius of the lateral canthus and minimally etched
3 (Moderate)	Moderately deep wrinkles, extending between 1.5- and 2.5-cm radius of the lateral canthus and moderately etched
4 (Severe)	Very long wrinkles, extending 2.5-cm radius of the lateral canthus and may be deeply etched

Source: Kane et al. *Aesthetic Surgery Journal*, 2012

When comparing the IGA with the FWS used in Allergan’s Botox studies, we believe that Revance’s methodology is less sensitive than those used in the clinical trials of FDA-approved products. On a four-point scale, as in the FDA-approved products, a greater than or equal to two-point improvement would indicate a greater increase than the same increase on the five-point scale used by Revance. In addition, there is a risk that the FDA would not consider a one-point improvement to be as significant in a five-point scale versus a four-point scale.



Despite the difference in scales, after speaking with a key opinion leader on efficacy measurements, there are several instances in the dermal filler market where five- and six-point scales were used in FDA-approved products. Juvederm Voluma, for example, was studied during follow-up visits at one, three, and six months after last treatment and assessed on a validated six-point photometric Mid-Face Volume Deficit Scale (MFVDS) by an investigator, as well as on a five-point Global Aesthetic Improvement Scale (GAIS) and a five-point Nasolabial Fold Photo Severity Scale (NLFSS) by the subject. In addition, Merz's Belotero product used the five-point Wrinkle Severity Rating Scale (WSRS) to assess efficacy (Day et al. *Am J Clin Dermatol*, 2004) and showed that intraobserver agreement was between 68.7% and 72.7%, with weighted kappa coefficients of 0.77 and 0.81.

The key opinion leader we spoke with on this subject stated that as long as the company has adequately shown that its scale has been properly validated and is reproducible (in the case of Revance, its scale has been published in peer-reviewed literature), the company should be able to get the product approved. According to the company's published study, Revance's five-point investigator scale showed an intrarater (same investigator scoring) weighted kappa score of 0.89 and an interrater (different investigators) weighted kappa score of 0.77 (Kane et al. *Aesthetic Surgery Journal*, 2012). To date, Revance has met with the FDA regarding its clinical program, and after a formal dispute resolution process, it believes it will receive approval for RT001 if its Phase III studies show efficacy and tolerability.

**Exhibit 3**  
**Summary of Select Rating Scales for Aesthetic Indications**

Scale Name	Product	Indication/Measurement Endpoint	No. of Points
Facial Wrinkle Scale (FWS)	Botox	LCL at maximum smile	4-point
Facial Wrinkle Scale (FWS)	Botox	GL at maximum frown	4-point
4-point scale	Dysport	GL at maximum frown	4-point
4-point scale	Xeomin	GL at maximum frown	4-point
Mid-Face Volume Deficit Scale (MFVDS)	Juvederm Voluma	Cheek augmentation to correct age-related volume deficit in mid-face of	6-point
Global Aesthetic Improvement Scale (GAIS)	Juvederm Voluma	adults over 21	5-point
Nasolabial Fold Photo Severity Scale (NLFSS)	Juvederm Voluma		5-point
Wrinkle Severity Rating Scale (WSRS)	Belotero	Smooth/fill nasolabial fold	5-point
Revance Facial Wrinkle Scale	Revance	LCL at rest	5-point

Sources: Company reports

## FDA Draft Guidance Continues Endpoint Debate

The recent issuance of draft guidance suggesting a maximum smile primary endpoint for trials developing botulinum toxin products for upper facial lines led to a significant decline in shares of Revance. The purpose of this endpoint, according to the agency, was to show that the toxin has a paralytic effect on muscle, or to paraphrase, the agency wanted to ensure products proved efficacy. In addition, the guidelines state that a demonstration of efficacy at the worst appearance of upper facial lines (at maximum contraction/smile) will allow for appropriate analysis of the aesthetic impact of treatment.

This differs from Revance's primary endpoint in its previous and current clinical programs of patients' and clinicians' assessments at rest. The FDA draft guidance follows a prior discussion between Revance and the agency during 2012 that resulted in a dispute resolution process, wherein the company proposed the primary efficacy point of change in LCL at rest. The outcome of this formal dispute favored Revance and the at-rest endpoint, which led to the company planning its Phase III program for RT001. While the company is examining the change in LCL at maximum contraction as a secondary endpoint, past data with this endpoint has been disappointing, and we do not expect this endpoint to reach statistical significance. The final assessment from the agency will depend

on a review of all data produced by Revance in the development of RT001, so the company should be in a strong position to argue the approvability of RT001, given over 2,000 patients' data to be produced by the time of submission. A key opinion leader that we spoke with also echoed what management has suggested, that improving LCL by using an at-rest endpoint would result in a more natural look, whereas oversmoothing LCL at maximal contraction may look "unnatural" and have a "dead eyes" impact.

Recently, a response to the FDA's draft guidance document was posted by three leading physicians, Dr. Brian S. Biesman, Dr. Richard G. Glogau, and Dr. Michael A. Kane. In this letter, the doctors highlighted two efficacy endpoint requirements that they felt required re-evaluation. Their points focused on the guidance to use measurements at maximum contraction being used to assess efficacy using a two-grade improvement from baseline on the investigator and subject assessment scales concurrently for clinical significance. The physicians stated in their response that dosing recommendations have trended downward in practice because of the need for assessing efficacy based on balancing diminished facial lines with maintaining a natural look, similar to the opinion expressed by the key opinion leader we previously spoke with.

The primary theme throughout the response was the need to define the success of botulinum toxin compounds from a real-world perspective instead of from a pure clinical trial perspective. In particular, the doctors wrote that each individual facial area has a unique function, emotion, and contribution to the facial whole, and no single treatment or assessment approach should be applied universally across all facial areas. Particularly with LCL, the response letter goes into depth on the reasons wrinkles at maximum contraction are important since they are present even in teenagers, whereas older patients typically seek treatment when LCL occurs at rest. Lastly, the physicians believe that a two-grade reduction in LCL at maximum contraction is another clinical endpoint that may not be beneficial in a real-world scenario. This is primarily because the orbicularis oculi muscle is very superficial, and a two-point required reduction in both scales concurrently would require an aggressive injection technique that may result in impairment or a "dropped smile" to the patient's natural smile. We believe these comments reflect our belief that the reaction to the release of the draft guidelines was largely overblown by investors, leading to a significant drop in share price. In addition, from talks with management, we also expect Revance to file a public response to the draft guidelines.

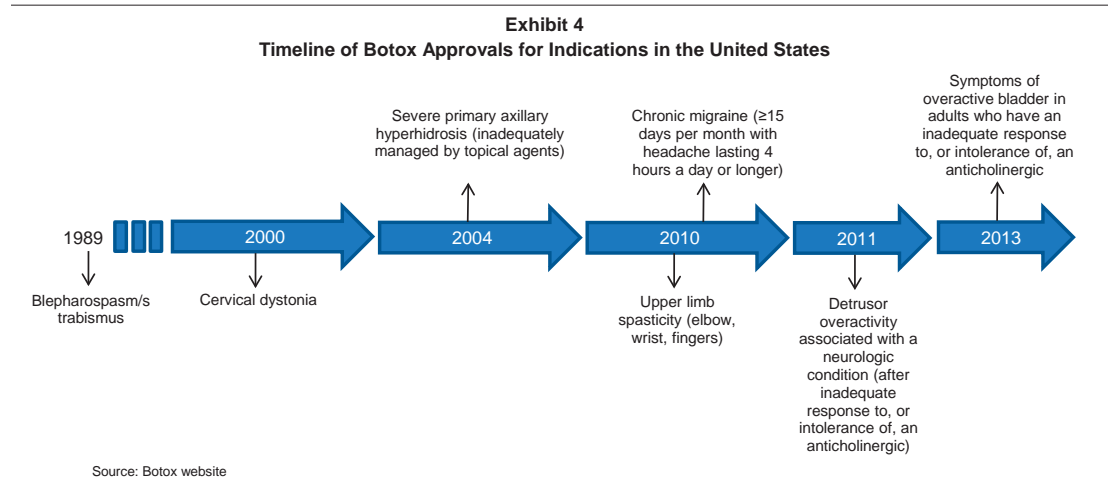
Management has consistently reiterated that it does not believe the draft regulatory guidelines will affect the company's regulatory submissions, and with the delay in the Phase III clinical program, we expect BLA and MAA submissions for RT001 by 2017. In the current form, the guidelines are more of a description of the agency's opinion on a certain topic at a certain point in time and should be viewed as recommendations, not hard rules. As a result of the agreed-on formal dispute resolution between the company and the agency in 2012, we also believe that the company will be able to proceed as planned. Our talks with several key opinion leaders, as well as the recent public response, give us confidence that the primary endpoint of LCL at maximal contraction will not affect Revance's current Phase III strategy of assessing LCL at rest. However, we believe this topic will likely be revisited on regulatory submission, and we believe data produced in the ongoing Phase III program will likely inform the next steps in the discussion of the endpoints used in the RT001 program, possibly during an advisory committee.



## Overview of Botulinum Toxin Type A

Botulinum neurotoxin is one of the most potent neurotoxins and is produced by the bacterium *clostridium botulinum*. Botulinum neurotoxins have seven different serotypes, lettered A through G, and are a class of large proteins that act via cholinergic neuromuscular junctions to block the transmission of synaptic vesicles (Jankovic, *Therapeutic Clinical Practice and Science*). The toxins are believed to produce this effect through a mode of action requiring four steps: binding to the receptors on the plasma membrane, penetrating the plasma membrane through receptor-mediated endocytosis, penetrating the endosomal membrane, and blocking exocytosis. In particular, serotype A, the serotype used in Botox, acts specifically on the synaptosome-associated protein SNAP-25.

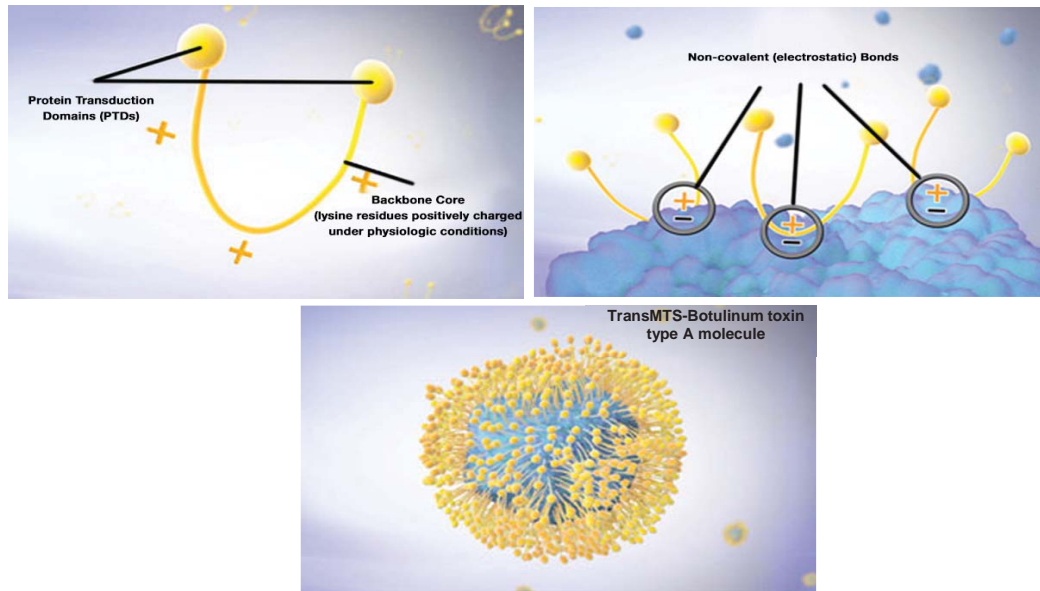
Allergan's Botox was initially approved in 1989 for use in blepharospasm, involuntary spasms of the eye, and strabismus, a condition in which the eyes are not properly aligned with one another. Since this initial indication, Botox has become one of the best-known brands in pharmaceuticals, and the current label includes more than 10 indications, spanning aesthetics, movement disorders, and the recent therapeutic indications of chronic migraine and overactive bladder. Exhibit 4 is a timeline of Botox U.S. approvals for different indications.



## Overview of TransMTS Peptide Technology

Revance's therapies in development use the company's proprietary TransMTS peptide delivery platform developed by co-founder and Chief Scientific Officer Jacob Waugh, M.D. The TransMTS peptide technology enables efficient transmembrane delivery of large molecules that would otherwise be more difficult to move intracellularly (in Revance's case, botulinum toxin type A). Exhibit 5, on the following page, details the composition of the TransMTS peptide delivery system with single, straight-chain peptides with two distinct domains: a backbone consisting of consecutive positively charged lysine residues and the protein transduction domain (PTD), which is responsible for delivery of the molecule to the target site. The PTD consists of transactivator of transcription (TAT) proteins that are also known as cell-penetrating peptides. These TAT proteins provide the ability to deliver large molecules that would otherwise not be able to bypass mammalian cell membranes into mammalian cells (Becker-Hapak et al., *Methods*, 2001). By more efficiently delivering the chemical to the site of administration, the company hopes to minimize the off-target effects of botulinum toxin by diffusion and subsequent inhibition of muscular contraction in adjacent tissues.

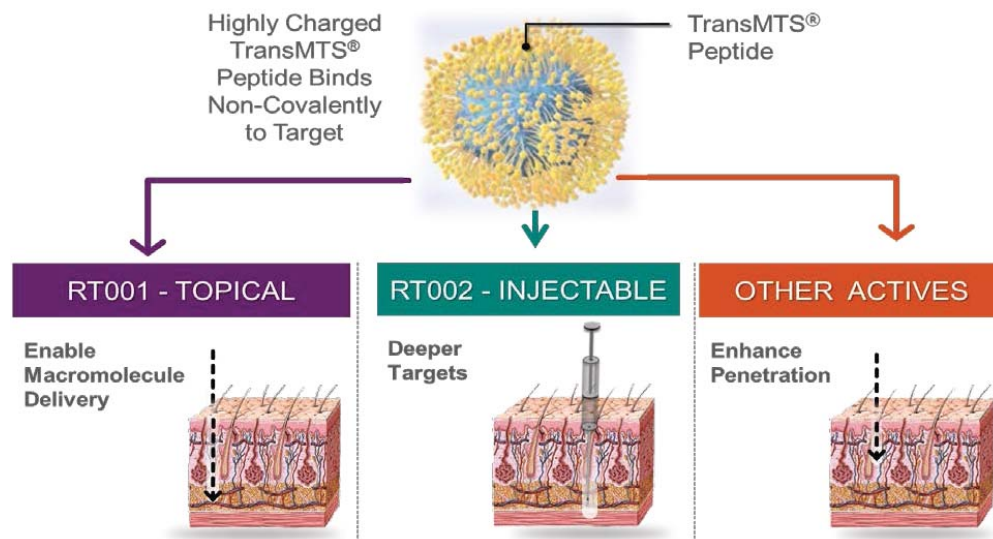
**Exhibit 5**  
**Revance Therapeutics, Inc.**  
**TransMTS Peptide Delivery System**



Source: Company website

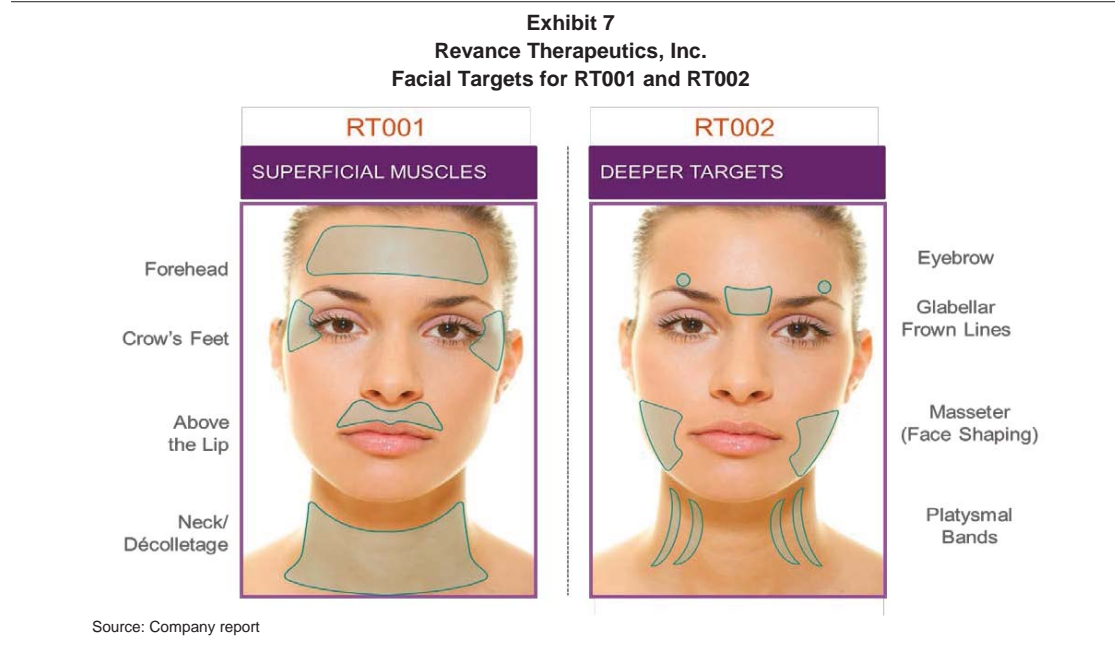
The positively charged lysine residues allow the TransMTS peptide to noncovalently bind to the target tissue (exhibit 6). For RT001, a topically delivered botulinum toxin type A, the peptide is delivered to the mid-dermis without an invasive injection process, which we believe could be an important delivery mechanism for patients who desire treatment but refuse to use injections. For RT002, a reduced-frequency injection of botulinum toxin type A, the peptide is delivered to deeper skin layers, such as the hypodermis.

**Exhibit 6**  
**Revance Therapeutics, Inc.**  
**TransMTS Peptide in Pipeline Products**



Source: Company report

Exhibit 7 shows particular areas of a patient's face that can be treated by RT001 and RT002. The skin above the lip (with lines referred to as smoker's lines) is a particular area where RT001 could be a preferred treatment as a result of the pain associated with injections. Injectable neurotoxins have also had mixed results near the mouth because of the risk of accidental paralysis and asymmetrical results, which are more apparent near the mouth than on other areas of the face, especially at rest and while smiling. In addition, the potential of a topical application could bring to the market many new patients who were previously not interested in facial injections or had facial bruising from prior injections.



Revance is focused on LCL for RT001 and on glabellar lines for RT002, so we believe the newly hired chief medical officer, Dr. Arthur P. Bertolino, will prioritize the next indications for both products. We expect an update over the next several quarters on the development path forward for new aesthetic and therapeutic indications.

## Pipeline Overview

Revance's pipeline is wholly focused on next-generation neuromodulators for aesthetic and therapeutic indications. There are many attractive attributes of the aesthetics market, in which there are few managed-care pressures in the largely cash-pay market catering to a desire for maintaining a youthful appearance among an aging population. According to the American Society for Aesthetic Plastic Surgery (ASAPS), consumers spent \$12.3 billion on 11.4 million physician-administered surgical and nonsurgical aesthetic procedures in the United States in 2013. Revance's pipeline consists of RT001 and RT002, with the primary indications of LCL (crow's feet) and of glabellar lines, respectively.

Exhibit 8 shows the stage of clinical development of both RT001 and RT002 for each of the potential indications to date. Given the large number of indications in which neuromodulators are used, we believe these first indications are only a starting point for development. In addition to further development, there is a common practice in aesthetics of using off-label neuromodulators, and we note the significant number of procedures for which botulinum toxin products have been approved in exhibit 9.

**Exhibit 8**  
**Revance Therapeutics, Inc.**  
**Product Portfolio Pipeline**

Indication	Preclinical	Phase I	Phase II	Phase III/ Pivotal	Comments/Timing
<b>RT001 - Topical Botulinum Toxin Type A</b>					
Lateral Canthal Lines (LCL or Crow's Feet)					Manufacturing confirmatory studies in early 2015, pending positive results, initiate Phase III program
Hyperhidrosis (Excessive Sweating)					Initiate Phase II study in 1Q15
Migraine Headache					
Other Therapeutic Indications					
<b>RT002 - Reduced Frequency Injectable Botulinum Toxin Type A</b>					
Glabellar Lines					Phase II trial versus Botox to be initiated in 4Q14, Interim results in 2H15
Therapeutic Indications					Initiate a Phase I/II study in a therapeutic indication in 2015

Sources: Company reports and William Blair & Company, L.L.C.

**Exhibit 9  
Botulinum Toxin Product Approvals**

<b>Indication</b>	<b>Year</b>
Blepharospasm	1989
Strabismus	1989
Cervical Dystonia	2000
<b>Glabellar Lines</b>	<b>2002</b>
Severe Axillary Hyperhidrosis	2004
Upper Limb Spasticity	2010
Chronic Migraine	2010
Neurogenic Overactive Bladder	2011
Idiopathic Overactive Bladder	2013
<b>Lateral Canthal Lines</b>	<b>2013</b>
Juvenile Cerebral Palsy	2014
Benign Prostatic Hyperplasia	2015

Source: Botox label

**Xeomin Approvals**

<b>Indication</b>	<b>Year</b>
Cervical Dystonia	2010
Blepharospasm	2010
<b>Glabellar Lines</b>	<b>2011</b>

Source: Xeomin label

**Dysport Approvals**

<b>Indication</b>	<b>Year</b>
Cervical Dystonia	2009
<b>Glabellar Lines</b>	<b>2009</b>

Source: Dysport label

**Botox Off-Label Potential Uses**

<b>Indication</b>
Headaches, except chronic migraines
Chronic low back pain
Joint pain
Mechanical neck disorders
Neuropathic pain after neck dissection
Myofascial pain syndrome
Pain after hemorrhoidectomy or lumpectomy
Tremors such as benign essential tremor
Tinnitus
Sialorrhea (except associated with Parkinson's disease)
Chronic motor tic disorder
Lateral epicondylitis
Benign prostatic hyperplasia
Interstitial cystitis
Detrusor sphincter dyssynergia
Piriformis
Prevention of pain associated with breast reconstruction after mastectomy
Hirschsprung's disease
Gastroparesis
Facial wound healing
Internal anal sphincter achalasia

Source: Blue Cross & Blue Shield

## RT001: Delays Have Been Frustrating, but Opportunity Keeps Development Moving Forward

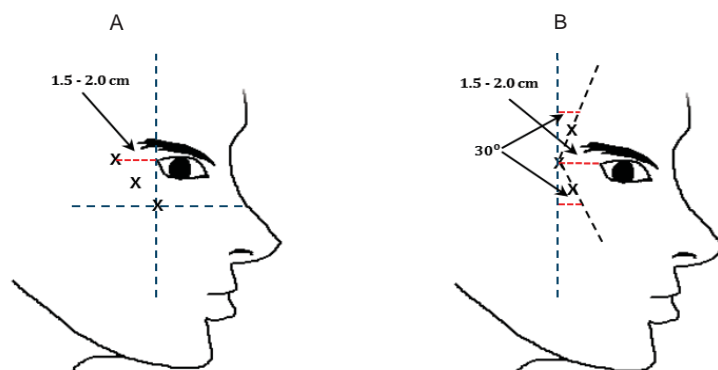
RT001 is a topically administered botulinum toxin type A in development for LCL, which has faced several delays, and hyperhidrosis, which may be the ideal indication for the product with significant differentiation from injectable products. We believe the potential for the product justifies continued investment despite multiple delays in the program, most recently following mixed results from a study to validate the efficacy of product manufactured internally. Botulinum toxin type A is the compound used in Allergan's successful Botox franchise, which accounted for about \$2 billion in revenue in 2013 in a \$2.8 billion neuromodulator market. We believe that a noninjectable version of botulinum toxin type A in RT001 has the potential to take significant market share after relatively undifferentiated products have already gained about 25% of the worldwide neuromodulator market and 15% of market share in the top-10 countries by sales. A topical product is also likely to expand the neuromodulator market into needle-phobic patients who are not already being treated.

### RT001 LCL Data to Date Shows Efficacy When Measured at Rest but Not While Smiling, Highlighting the Need for End-Point Resolution

The initial indication for which RT001 has been developed to date has been LCL (crow's feet), which is defined by skin wrinkles in the corner of the eye and is most commonly associated with aging. According to data presented previously by Allergan, while Botox injections are the largest aesthetic procedure performed in the United States, injectable neurotoxins, such as Botox, are used by only 10% of U.S. consumers. When Allergan expanded the Botox labeling to include LCL, management had noted its expectation for this indication to lead to an incremental \$100 million in worldwide sales; however, we believe this number did not include the significant off-label use of Botox in this indication already captured within Botox sales figures.

Botox involves several steps in the preparation of the product from dry to liquid form and requires administration by a dermatology practice. First, 24 units of dry Botox Cosmetic are mixed in 0.6 ml of sterile preservative-free 0.9% saline solution in a 4 units/0.1 mL ratio. The mixture is then drawn into a syringe and administered using a 30-33 gauge needle. For LCL, Botox is injected into three sites per side (a total of six injection points) in the lateral orbicularis muscle. According to the product label, the first injection should be approximately 1.5-2.0 cm temporal to the lateral canthus and just temporal to the orbital rim. If the lines in the lateral canthal region are above and below the lateral canthus, injections should be given as shown in exhibit 10A; if the lines in the lateral canthal region are primarily below the lateral canthus, they should be injected as shown in exhibit 10B.

**Exhibit 10**  
**Botox Injection Sites for LCL**



Sources: Allergan company reports and William Blair & Company, L.L.C.



After speaking with a dermatologist consultant, we believe that the majority of Botox applications for LCL are performed on a patient-by-patient basis, and most do not follow the label indication for injection sites. This is primarily because of the potential to “drop an eyelid” (having the Botox diffuse into the superficial eyelid) or “drop a smile” (injecting too low on the individual’s face, thereby affecting the zygomaticus muscles). In addition, there are different approaches taken by dermatologists to inject patients for LCL. One approach is to use fewer injections and more units and manually spread the botulinum toxin to the appropriate areas. Another approach is to use more injections and fewer units, primarily to have more control on the sites of application if the patient’s LCL are more spread out. However, for both approaches, patients are initially asked to squint or perform a maximum smile to locate the LCL before injection, therefore making LCL during contraction a key indicator of need for retreatment. This gives us some concern regarding the potential of RT001 to penetrate the patient population, if approved.


Lastly, regarding the amount, our consultant also stated that the approved dosing of 24 units is particularly high for the orbicularis oculi, a particularly weak muscle, and believes that the majority of dermatologists use 6 to 10 (at the very most) units per eye with an effect seen within five to seven days and maximum effect at two weeks post-injection. A study examined the consensus recommendations on the aesthetic usage of botulinum toxin in an Asian population and found that for LCL, dermatologists recommended three injections per side (7 units/side) at the lateral part of the orbicularis oculi for a total of 14 units (Ahn et al. *Dermatologic Surgery*, 2013). Also, dermatologists we spoke with stated that gender could also determine injection volume. Therefore, the demographic of the patient can play a significant role in the amount injected.

#### **Easy RT001 Administration Could Be a Differentiator**

In contrast to the preparation and administration of Botox, RT001 is administered by preparing an applicator with a cartridge that contains a gelatinous form of TransMTS and botulinum toxin type A. The topical formulation is then applied in a two- to three-minute process. After application, there is a 30-minute dwell time and the formulation is then easily removed using gentle cleansing wipes, followed by a short deactivation process. The total process does not take longer than an hour and can be performed by medical personnel other than dermatologists and plastic surgeons, such as nurses. The dilution and administration of RT001 is a key differentiator from Botox. There may be some consistency differences among personnel performing the procedure with Botox because of the mixing and preparation of the dry Botox powder. As shown in exhibit 11, on the following page, the applicator for RT001 enables simple loading, usage, and discarding that gives it an advantage over other competitors (i.e., Botox, Dysport, and Xeomin) that require experience and practice.

Exhibit 12 shows sample patients before and after treatment with RT001, along with example images of the 1- and 2-point scale that physicians used to measure patients in the company’s clinical trials. This example shows the improvement observed when at rest after only a single treatment. While we believe that these examples show the obvious improvements that are possible to observe using the at-rest endpoint, there is still controversy surrounding this endpoint because the ability to change superficial wrinkles in the epidermis seen during the at-rest period may not have an effect or the effect may be shorter in duration due to the deeper layers of skin and musculature that cause wrinkles seen at maximum smile.

Exhibit 11  
Revance Therapeutics, Inc.  
Preparation of RT001 Applicator for Lateral Canthal Lines




RAA Components	Activation/Reconstitution	Draw Up Dose/Apply
RT001 topical gel is provided in a ready-to-use format (1) with drug vial and diluent cartridge pre-assembled in a reconstitution, activation, and application (RAA) device.	RAA is first activated (2); this establishes the fluid path between the diluent cartridge and drug vial. Plunger rod is then inserted (3) and depressed to transfer diluent to drug vial for reconstitution.	Dose is drawn into cartridge (4), vial socket is removed, and the dose is ready to apply (or can be stored for up to 8 hours before application).

Source: Company reports

Exhibit 12  
Revance Therapeutics, Inc.  
Validated Clinical Improvement Scale of RT001

1-POINT IMPROVEMENT



Baseline (Pretreatment)4 Weeks Post-treatment (Single Treatment)

2-POINT IMPROVEMENT



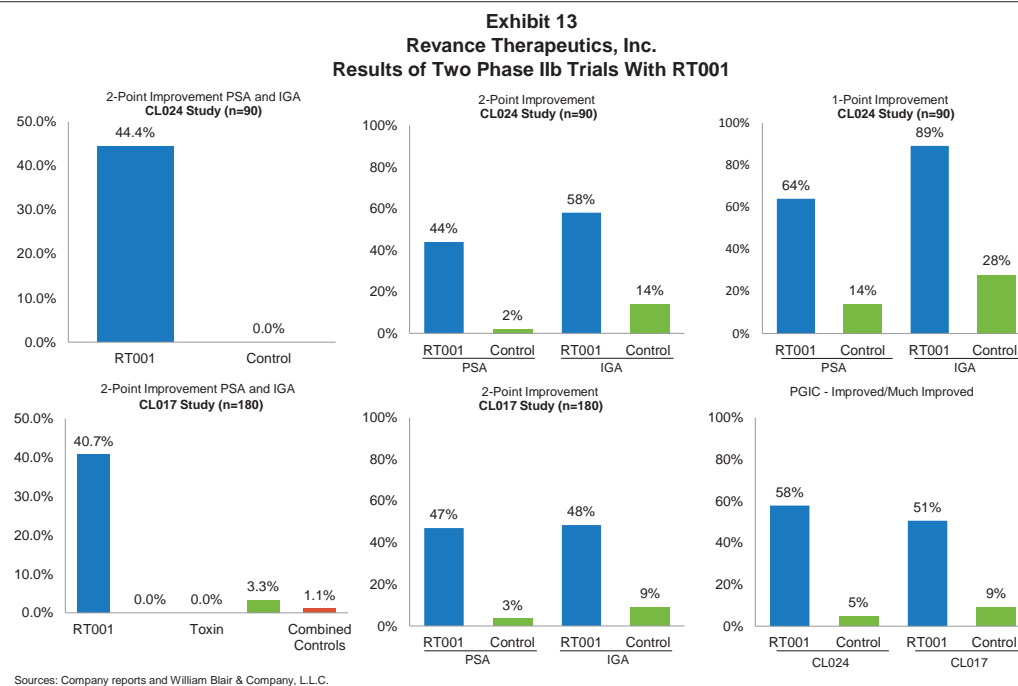
Baseline (Pretreatment)4 Weeks Post-treatment (Single Treatment)

Source: Company report

### Phase II Data in LCL Suggests Efficacy at Rest, but More Natural Effect Is Not Captured by Maximum-Smile Endpoint

The company's data for RT001 in LCL includes two Phase IIb studies, CL017 (n=180) and CL024 (n=90), using a dose of 25 ng/ml. CL017 was designed to measure the impact of a single treatment of RT001 on LCL based on the IGA and a patient severity assessment (PSA) of LCL after four weeks of treatment. CL024 was designed with four cohorts randomized 1:1:1:1, botulinum toxin alone, peptide alone, and placebo for both IGA and PSA, to control for each individual component of RT001.

As shown in exhibit 13, the percentage of two-point improvement in PSA and IGA combined was 44.4% in CL024 and 40.7% in CL017. In CL024, the percentage of patients with one-point improvement was stratified into PSA and IGA, with 64% in RT001 versus 14% in the control for PSA ( $p<0.0001$ ), and 89% in RT001 versus 28% in the control population for IGA ( $p<0.0001$ ). Regarding duration of effect, combining the results of CL017 and CL024, RT001 was measured to be effective for 83 days (as assessed from a change from a two-point response to a one-point response) and 113 days (as assessed from a change from a one-point response back to baseline response). This is consistent with the duration of effect of the current market leaders, with Botox lasting about three to four months, according to the label. The effect of Botox Cosmetic administration more frequently than every three months has not been clinically evaluated; however, after speaking with a dermatologist consultant, certain active patients with higher metabolisms have been thought to have an effect of only one and a half to two months as well.



With more than 1,030 patients tested to date, the safety profile of RT001 was very impressive with no related significant adverse events (AEs), no subjects discontinuing as a result of AEs, no significant regional spread of botulinum toxin from the application site, and no systemic risk based on electrocardiograms or clinical laboratory results. This safety data could be a rather important consideration for patients who have interest in a botulinum toxin injection but are afraid of the AEs associated with injections and diffusion of the product to adjacent tissues.

**Previous Phase III Study Results Were Negatively Affected by a Formulation Change That Was Subsequently Found to Be Unnecessary**

Based on the results from its Phase IIb studies, the company moved into a Phase III trial for RT001 in LCL. Before the initiation of the Phase III trial, however, the company changed the formulation of RT001 by adding two ingredients (a preservative called butylated hydroxytoluene, or BHT, and ethanol) with the intention of increasing the stability of the product to increase shelf-life.

In the Phase III study with the new formulation, the p value of the trial was 0.997, almost completely in line with the placebo. We find this result plausible evidence that the formulation caused serious issues with the efficacy of RT001 as a result of the extreme difference between the Phase III results and previous clinical studies reported by the company. During the Phase III study, the company received two-year stability data from the original Phase II formulation, suggesting that the reformulation between Phase II and Phase III was not necessary. The company has reverted to the original formulation from the Phase IIb studies for its new Phase III clinical trial program, and we believe this will lead to larger differences from placebo in its trials.

**Two-Cohort Phase II Study Complicated by Error, but Cohort 2 Was Positive**

To ensure that the negative result in the Phase III trial was due to the new formulation (with BHT and ethanol), the company initiated a small Phase IIb efficacy study with the old formulation. The study, labeled CL035, enrolled two cohorts; however, this study was negatively affected by a randomization error caused by a lab technician who misplaced a treatment cycle with a placebo cycle, which then affected subsequent dosing of patients. When correcting for that error, cohort 1 (n=42) showed a significant difference in the primary endpoint of composite scores  $\geq 2$ -point with a 23.8% response, versus 0% in placebo (p=0.017).

Cohort 2 added 40 patients to the initial 42 from cohort 1 to confirm the randomization error had occurred with cohort 1. The second cohort individually showed statistical trends in line with cohort 1 after correcting for the randomization error with IGA (at rest)  $\geq 2$ -point, p=0.13; IGA (at rest)  $\geq 1$ -point, p=0.019; PSA  $\geq 2$ -point, p=0.53; IGA (smile)  $\geq 1$ -point, p=0.002; and IGA (smile)  $\geq 2$ -point, p=ns. The corrected analyses of the combined study shown in exhibit 14 have significant increases in several of the endpoints, including the primary endpoint of composite scores  $\geq 2$ -point with 22% response versus 4.9% in placebo (p=0.024), IGA at rest scores  $\geq 2$ -point at 41.5% response versus 12.2% in placebo (p=0.0003), IGA at rest scores  $\geq 1$ -point having 63.4% response versus 41.5% in placebo (p=0.047), and IGA with smile scores  $\geq 1$ -point showing 68.3% response versus 34.1% in placebo (p=0.0002).

In exhibit 14, we have noted that in CL035, when all errors were corrected for in the combined study, the  $\geq 2$ -point IGA scores at maximum smile were not significant from placebo versus the  $\geq 2$ -point IGA at rest. The company may need additional FDA support or potentially an advisory committee meeting to support the at-rest endpoint. However, the Dermatologic and Ophthalmic Drugs Advisory Committee (DODAC) rarely meets for dermatologic purposes; the last meeting was in 2011 regarding Accutane causing severe adverse events. Although the company has undergone formal dispute resolution meetings with the FDA specific to RT001, we believe that the inability to improve LCL as assessed by investigator global assessment at maximum smile may affect market penetration rates, assuming the product gets approval, based on a significant difference at rest.

**Exhibit 14**  
**Revanche Therapeutics, Inc.**  
**Results of CL035 Clinical Trial on Efficacy of RT001 in Crow's Feet Lines**

Endpoint	Group	First Cohort (42 patients)			Combined Study (82 patients)		
		Response (%)	p-value	Change in Treatment vs. Placebo	Response (%)	p-value	Change in Treatment vs. Placebo
Composite ≥2-point	RT001	23.8			22		
	Placebo	0	0.017	23.8	4.9	0.024	17.1
IGA (Rest) ≥2-point	RT001	52.4			41.5		
	Placebo	14.3	0.009	38.1	12.2	0.0003	29.3
IGA (Rest) ≥1-point	RT001	57.1			63.4		
	Placebo	47.6	NS	9.5	41.5	0.047	21.9
PSA ≥2-point	RT001	38.1			39		
	Placebo	19	0.17	19.1	24.4	0.15	14.6
IGA (Smile) ≥1-point	RT001	57.1			68.3		
	Placebo	38.1	0.36	19	34.1	0.0002	34.2
IGA (Smile) ≥2-point	RT001	4.8			4.9		
	Placebo	0	NS	4.8	4.9	NS	0

Sources: Company reports and William Blair & Company, L.L.C.

≥2-point IGA at rest was significant in both the first cohort and combined study.

≥2-point IGA at maximum smile was not significant in either the first cohort or the combined study.

### New Process to Be Confirmed in Phase II; Phase III Program Initiation on Hold

After several clinical setbacks, the company underwent a 43-patient Phase II trial to confirm successful verification/scale up of RT001 before initiating Phase III studies for LCL, which we outline in exhibit 15. Unfortunately, on its latest earnings call, the company stated that in an interim analysis of the 32 patients, it received encouraging results in the PGA and IGA assessments separately, but that the two-point response rate results were not consistent with the results from its Phase II program (CL017, CL024, and CL035). The company expects to manufacture additional RT001 product at its manufacturing facility and conduct a second open-label Phase II trial in early 2015. While we are a bit frustrated by yet another setback in the RT001 program, the company is taking careful steps now to ensure that its large Phase III program will have a high probability of success. Investors must wait until the first quarter of 2015 for an updated timeline of its Phase III program; however, we believe that a one-quarter delay in the Phase III program may push the NDA and MAA submissions for RT001 into 2017.

Pending positive results from the most recent Phase II trial to confirm the efficacy of the scale-up manufactured product, Revance will initiate its broad Phase III program for RT001. Management had previously articulated that the Phase III program will include two pivotal Phase III trials in the United States and will use the same study design and primary endpoint: the efficacy of a single administration compared with placebo using an IGA and two-point improvement from baseline (at rest, not maximal smile) with follow-up for about 150 days.

Revanche will also conduct another pivotal Phase III trial in Europe to support an MAA application, with the EU trial evaluating safety and efficacy of RT001 compared with placebo after a single administration and a shorter three-month safety follow-up. Lastly, the company has initiated a long-term open-label Phase III safety trial that will evaluate multiple treatment cycles with repeat dosing when subjects revert to moderate-to-severe crow's feet lines at intervals of 90 days or greater. The study will allow up to two years of treatment with up to four exposures per year and will evaluate adverse events, rare events, and safety of repeat dosing over multiple cycles.

For its eventual BLA submission, the company expects to have studied more than 2,000 patients at dosage levels intended for commercial usage, with roughly 1,800 of those patients having been dosed for six months and the majority of those patients having received multiple cycles of treatment. In addition, the company anticipates about 300 subjects will have been treated for 12 months with three to four treatment cycles.

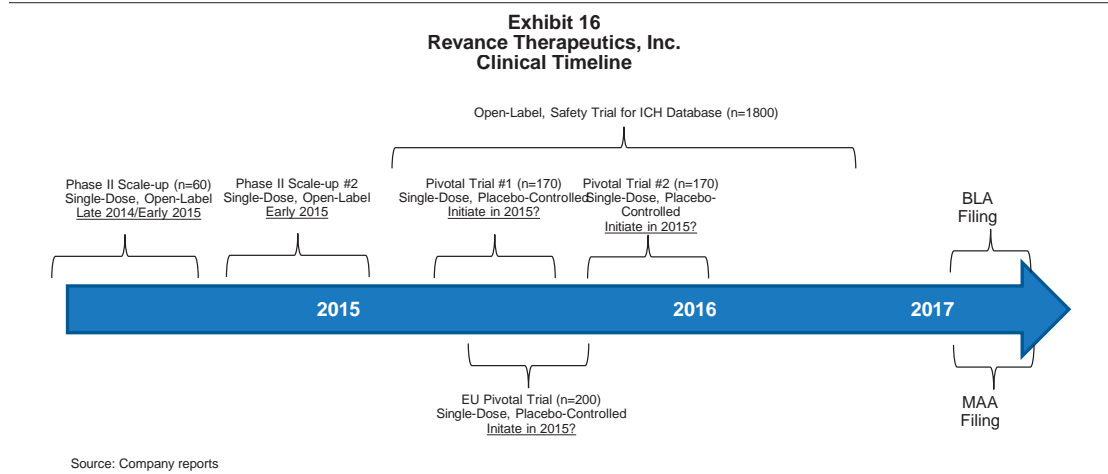
**Exhibit 15**  
**Revance Therapeutics, Inc.**  
**Global Phase III Program for RT001 in Crow's Feet Lines**

Trial	Timeline	Trial Type	Estimated Number of (Trial Location)	Purpose	Dose	Endpoint(s)	Estimated Data Availability
Two Open-Label Confirmatory Studies	Started in 3Q 2014	Single Dose	Up to 60 (U.S.)	To confirm success of the production transfer of RT001 to Revance commercial manufacturing facilities	25 ng/mL	Primary: investigator and patient assessments at rest; secondary endpoints include investigator/patient assessments at maximum smile	Interim readout in 3Q 2014; full data in early 2015; second open-label confirmatory study in early 2015
Phase III Pivotal Trial No. 1	TBD	Single-Dose, Placebo-Controlled	170 (U.S.)	To evaluate efficacy and safety of RT001 after single administration compared with placebo	25 ng/mL; follow-up for roughly 150 days to evaluate duration of response	Primary: investigator and patient assessments at rest; secondary endpoints include investigator/patient assessments at maximum smile	TBD
Phase III Open-Label Trial	Started in 2014	Open-Label, Repeat Dose	1,800 New and Rollover Subjects (U.S.)	Long-term safety assessment of RT001 with multiple treatments	25 ng/mL; up to two years of treatment with up to four exposures per year	Late onset adverse events, rare events, and repeat doses over multiple cycles	2015 (interim data)
Phase III Pivotal Trial No. 2	TBD	Single-Dose, Placebo-Controlled	170 (U.S.)	To evaluate efficacy, safety, and duration of RT001 after single administration compared with placebo	25 ng/mL; follow-up for roughly 150 days to evaluate duration of response	Primary: investigator and patient assessments at rest; secondary endpoints include investigator/patient assessments at maximum smile	TBD
Phase III Pivotal Trial No. 3	TBD	Single-Dose, Placebo-Controlled	200 (Europe)	To evaluate efficacy, safety, and support EU marketing applications	25 ng/mL; three-month follow-up for safety	Primary: investigator and patient assessments at rest; secondary endpoints include investigator/patient assessments at maximum smile	TBD

Sources: Company reports and William Blair & Company, L.L.C.

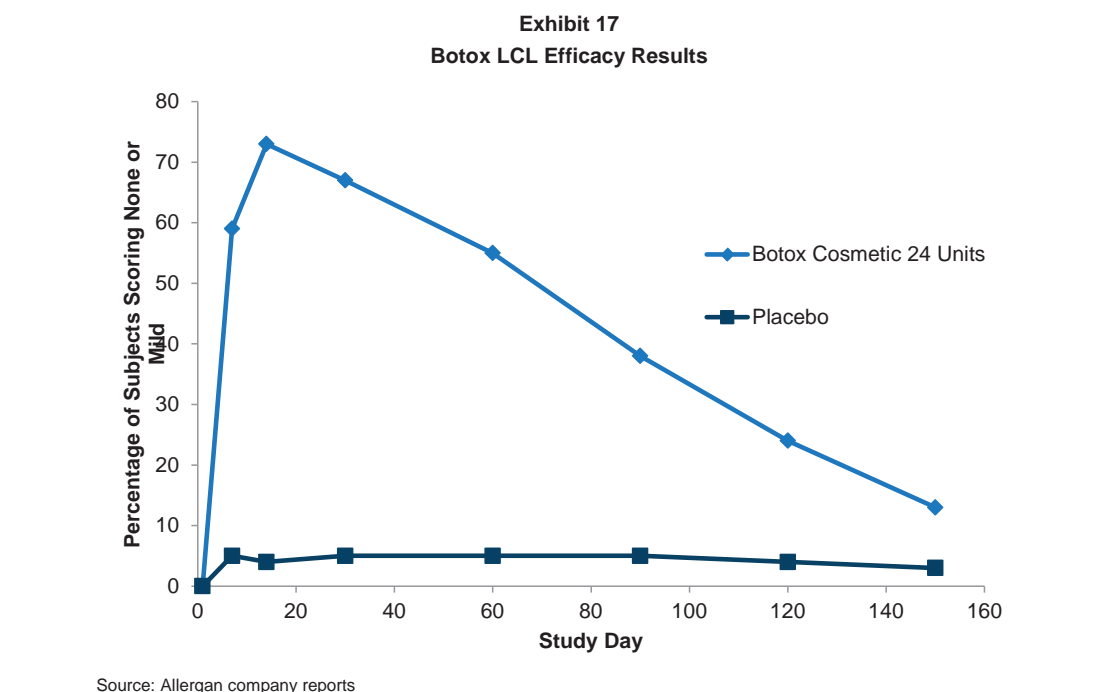


Our expected timeline for the Phase III clinical trial program launch, interim data analysis, completion, expected BLA/MAA submission, and potential commercial launch in the United States and Europe is provided in exhibit 16. However, it should be noted that this timeline is based on the results of the Phase II confirmatory studies from the company to be reported in early 2015.



### RT001 Efficacy Does Not Compare With Botox Data, Because of Differences in Composite Endpoint

According to the label for Botox Cosmetic, the compound is indicated for the temporary improvement in the appearance of moderate-to-severe LCL associated with orbicularis oculi activity in adult patients. As shown in exhibit 17 from the Botox clinical trial assessing treatment over a five-month period, the percent of subjects scoring none or mild LCL (at maximal smile) after treatment with 24 units was significantly different from placebo (about 72% Botox versus about 4% placebo at peak efficacy on day 14). By day 30, the percentage in Botox-treated patients was slightly reduced to 68% (compared with about 6% in placebo) and continued to decline thereafter to less than 20% by day 150.



In this five-month study, the primary endpoint was the composite investigator and subject assessment of LCL assessed at maximum smile on day 30 of the study. A responder was classified as the percentage of subjects achieving a greater than two-grade improvement from baseline. The responder rate was 26.1% in the Botox group and 1.3% in the placebo group. These results cannot, however, be directly compared with results coming out of the RT001 program given the composite endpoint. While RT001 has a well-documented effect when measuring wrinkles at-rest, which we have described previously, the compound does not show clear differences when patients are measured at maximal smile.

### Hyperhidrosis: Perhaps the Ideal Topical Indication; Proof of Concept in 2015

In addition to the primary indication of LCL, RT001 has also been tested for the indication of hyperhidrosis, or excessive sweating. Given the anatomy of the skin with both sweat glands and sweat ducts relatively close to the surface, this indication may prove to be the ideal setting for a product like RT001. The market is large; hyperhidrosis affects about eight million people in the United States (one million with severe hyperhidrosis), and only 38% of those affected currently seek treatment. Exhibit 18 shows a 2004 survey by the International Hyperhidrosis Society that provides available treatment options for hyperhidrosis.

**Exhibit 18**  
**Survey of Currently Available Treatments Used for Hyperhidrosis**

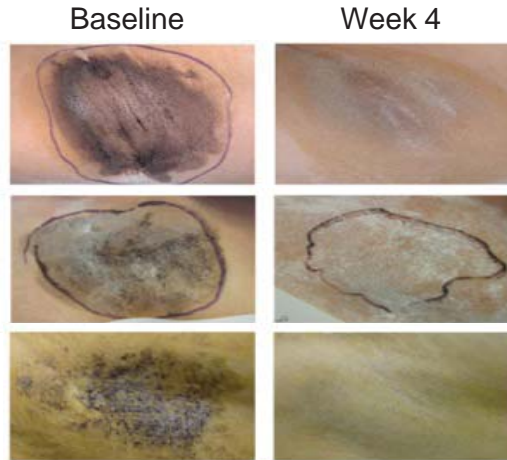
Treatment	Percentage of Respondents
Prescription antiperspirants	64%
Over-the-counter antiperspirants	42%
Oral medication	27%
Iontophoresis	13%
Botox injections	8%
Surgery	6%

Sources: International Hyperhidrosis Society, company reports, and William Blair & Company, L.L.C.

Revanche has completed an initial Phase II dose-escalation study for the indication. To test for sweat in the study, the patient's skin was initially treated with an iodine solution that was allowed to dry and followed by dusting of corn starch and sweat assessment period of 10 minutes. If sweat occurred, the starch and iodine would dissolve and the reaction would form a dark staining pattern. Subjects were randomized to receive a single treatment of RT001 or placebo and followed for four weeks (28 days) after treatment. Exhibit 19 shows results of baseline and after week four of treatment. The company plans to initiate further clinical trials starting with an efficacy trial of a high dose (25 ng/mL) to determine whether it is an adequate dose to advance further, and we expect an update regarding the initiation of this trial in early 2015.

Revanche management will initiate an additional Phase II study in early 2015 with doses and procedures that are specific to the hyperhidrosis indication. The company will share with the Street the details of the trial design when they are finalized and the trial is launched during the first quarter of 2015. Botox has shown to be effective in the treatment of hyperhidrosis with 55% response rates (Botox 50 units) and 49% (Botox 75 units) versus 6% response rates in those treated with a placebo. In the Botox HH studies, response was defined as showing, in the patient questionnaire the Hyperhidrosis Disease Severity Scale (HDSS), 2 or more grades of improvement after four weeks from two treatment sessions. Despite the efficacy of Botox in this indication, we do not believe the product is even close to tapping the potential in this market, given the large number of patients and the difficult administration of the injectable products in this patient population. The indicated administration for Botox for HH included in the therapeutic label suggests 10-15 injections spaced 1 cm-2 cm apart. We believe this will be especially unpleasant for patients who experience HH on their hands, feet, and underarms. If RT001 demonstrates positive proof-of-concept data in this indication, we believe this may be the ideal setting for a topically administered product.

**Exhibit 19**  
**Revance Therapeutics, Inc.**  
**RT001 Starch Iodine Results in Hyperhidrosis From Phase II Study**



Source: Company report

**Migraine Headaches: Potential Therapeutic Indication for RT001 That Could Provide Another Avenue for Penetration of the Botox Franchise**

While we believe that Revance is weighing development options for both RT001 and RT002, another possible major indication for RT001 could be migraine headaches, for which Botox was approved in 2010. The Migraine Research Foundation estimates that this condition results in 113 million lost workdays and costs employers about \$13 billion each year. Exhibit 20 details several facts about the migraine market. Although the data is dated (published in 1997), Dr. Richard Lipton of the Albert Einstein College of Medicine demonstrated that migraines affect up to 18% of women and 6% of men in the United States, with a peak incidence between 25 and 55 years of age (Lipton RB, *Neurologic Clinics*).

The American Academy of Neurology states that chronic migraine affects 3.2 million Americans, a market eight times larger than that for multiple sclerosis, another neurology market in which biologic therapies have launched significant products over the past 10-15 years. Roughly three million patient visits to emergency departments each year are attributed to migraines.

**Exhibit 20**  
**Migraine Facts**

- Disabling headache pain lasting 4 to 72 hours
- 75% of patients are women
- Ninth-leading cause of disability in women worldwide
- Seventh-most-costly disease to U.S. employers
- Estimated \$25 billion annual cost to employers
- 63% of patients suffer one or more attack each month
- 48% of patients experience symptoms after waking in the morning (between 4:00 a.m. and 9:00 a.m.)
- 29% of sufferers reported vomiting as a symptom

Sources: National Headache Foundation, World Health Organization, Goetzel et al. *JOEM* (2004), International Headache Society, Thomson Medstat (2006), Lipton et al., *Neurology* (2002), and company reports

Botox was approved for the treatment of chronic migraine headaches in 2010; however, the Botox treatments require 31 different injections at different sites in the patient's head, as detailed in exhibit 21. Despite the difficulties in Allergan's attempts to receive approval for Botox for chronic migraine, we believe that the involved injection process for Botox could be an entry point for RT001 into the therapeutic category.

**Exhibit 21**  
**Botox Dosing by Muscle for Chronic Migraine**

Head/Neck Area	Recommended Dose (Number of Sites <sup>a</sup> )
Frontalis <sup>b</sup>	20 units divided in 4 sites
Corrugator <sup>b</sup>	10 units divided in 2 sites
Procerus	5 units in 1 site
Occipitalis <sup>b</sup>	30 units divided in 6 sites
Temporalis <sup>b</sup>	40 units divided in 8 sites
Trapezius <sup>b</sup>	30 units divided in 6 sites
Cervical Paraspinal Muscle Group <sup>b</sup>	20 units divided in 4 sites
<b>Total dose:</b>	<b>155 units divided in 31 sites</b>

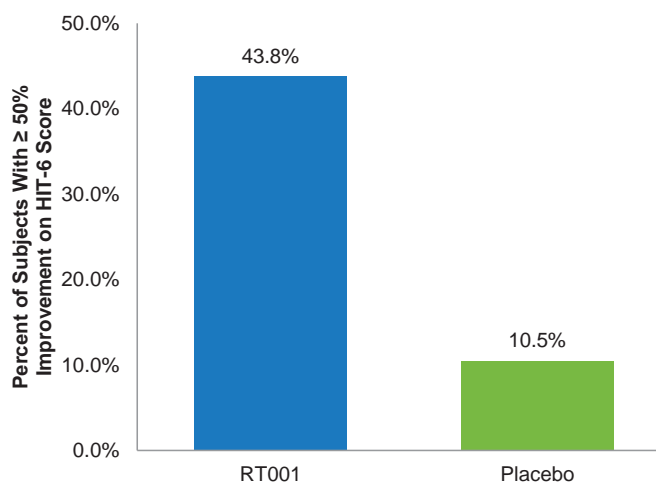
<sup>a</sup> Each IM injection site = 0.1 mL = 5 units of Botox

<sup>b</sup> Dose distributed bilaterally

Sources: Botox product label and William Blair & Company, L.L.C.

Revance completed a double-blind proof-of-concept study in 35 patients that achieved its primary endpoint of patients with an improvement of  $\geq 50\%$  in the Headache Impact Test-6 (HIT-6), from 10.5% in placebo, to 43.8% in RT001 ( $p=0.0498$ ). See exhibit 22.

**Exhibit 22**  
**Revance Therapeutics, Inc.**  
**RT001 Proof-of-Concept Study in Migraine: Phase I/II Results**



Sources: Company reports and William Blair & Company, L.L.C.

**Exhibit 23**  
**Pooled Results From Pivotal PREEMPT Program**

	Week 24				Week 56			
	Botox (n=688)	Placebo (n=696)	Mean intergroup difference	P Value	Botox (n=688)	Placebo (n=696)	Mean intergroup difference	P Value
Change from baseline in mean frequency of headache days	-8.4 (-8.90, -7.92)	-6.6 (-7.07, -6.08)	-1.8 (-2.52, -1.13)	<0.001	-11.7 (-12.17, -11.20)	-10.8 (-11.32, -10.31)	-0.9 (-1.53, -0.14)	0.019
Change from baseline in mean frequency of migraine days	-8.2 (-8.69, -7.70)	-6.6 (-7.07, -6.08)	-1.8 (-2.52, -1.13)	<0.001	-11.7 (-12.17, -11.20)	-10.8 (-11.32, -10.31)	-0.9 (-1.53, -0.14)	0.019
Change from baseline in mean frequency of moderate/severe headache days	-7.7 (-8.22, -7.27)	-5.8(-6.28, -5.30)	-1.9(-2.62, -1.26)	<0.001	-10.7 (-11.18, -10.25)	-9.9 (-10.43, -9.44)	-0.8 (-1.41, -0.09)	0.027
Change from baseline in cumulative total headache hours on headache days	-119.7 (-129.58, -109.76)	-80.5 (-90.56, -70.42)	-39.2 (-48.40, -21.04)	<0.001	-169.1 (-179.30, -158.81)	-145.7 (-155.94, -135.36)	-23.4 (-29.15, -2.78)	0.018
<b>Percent of patients with severe (≥60) HIT-6 score</b>	<b>67.6% (64.1%, 71.1%)</b>	<b>78.2% (75.1%, 81.2%)</b>	<b>-10.6% (-15.2%, -5.9%)</b>	<b>&lt;0.001</b>	<b>50.6% (46.9%, 54.3%)</b>	<b>51.9% (48.2%, 55.6%)</b>	<b>-1.3 (-6.6%, 4.0%)</b>	<b>0.632</b>
Change from baseline in mean frequency of headache episodes	-5.2 (-5.61, -4.84)	-4.9 (-5.32, -4.53)	-0.3 (-1.17, -0.017)	0.009	-7.4 (-7.79, -6.97)	-7.5 (-7.91, -7.09)	0.1 (-0.87, -0.04)	0.075
Change from baseline in mean frequency of migraine episodes	-4.9 (-5.25, -4.50)	-4.5 (-4.90, -4.12)	-0.4 (-1.20, -0.23)	0.004	-6.8 (-7.21, -6.43)	-7.0 (-7.37, -6.58)	0.2 (-0.80, -0.09)	0.117
Change from baseline in mean frequency of acute headache medication intakes (all categories)	-10.1 (-11.37, -8.81)	-9.4 (10.62, -8.13)	-0.7 (-2.68, 0.69)	0.247	-15.4 (-16.74, -14.05)	-15.7 (-17.05, -14.33)	0.3 (-1.76, -1.29)	0.760
Change from baseline in mean frequency of triptan intakes	-3.2 (-3.63, -2.71)	-2.1 (-2.57, -1.58)	-1.1 (-1.74, -0.61)	<0.001	-4.2 (-4.69, -3.67)	-3.8 (-4.35, -3.27)	-0.4 (-1.02, -0.06)	0.08
Change from baseline in mean frequency of acute headache medication days	-6.1 (-6.58, -5.54)	-5.3 (-5.77, -4.75)	-0.8 (-1.53, -0.15)	0.016	-8.4 (-9.08, -7.79)	-8.5 (-9.16, -7.82)	0.1 (-1.19, 0.46)	0.69
<b>Change from baseline in total HIT-6 scores</b>	<b>-4.8 (-5.34, -4.29)</b>	<b>-2.4 (-2.85, -1.95)</b>	<b>-2.4 (-3.11, -1.72)</b>	<b>&lt;0.001</b>	<b>-7.7 (-8.24, -7.06)</b>	<b>-7.0 (-7.62, -6.40)</b>	<b>-0.6 (-1.49, 0.20)</b>	<b>0.069</b>
Change from baseline in MSQ score								
Role restrictive	17.0 (18.75, 15.21)	8.6 (10.18, 7.00)	8.4 (10.76, 6.01)	<0.001	25.2 (27.27, 23.08)	21.8 (23.93, 19.63)	3.4 (6.41, 0.39)	0.043
Role preventive	13.1 (14.83, 11.37)	6.4 (7.98, 4.85)	6.7 (9.01, 4.35)	<0.001	19.0 (21.06, 17.01)	17.3 (19.40, 15.26)	1.7 (4.60, 1.20)	0.293
Emotional function	17.9 (20.09, 15.79)	9.5 (11.43, 7.53)	8.4 (11.37, 5.56)	<0.001	25.0 (27.41, 22.60)	22.1 (24.66, 19.62)	2.9 (6.36, -0.62)	0.51

Sources: Aurora SK, *Headache* 2011, and William Blair & Company, L.L.C.

In Allergan's pivotal PREEMPT program, shown in exhibit 23, at week 24, Botox showed a reduction in the percent of patients with severe HIT-6 scores compared with placebo of about 11% (67.6% Botox versus 78.2% placebo). Botox also showed an increased change from baseline in total HIT-6 scores from -2.4 in placebo, to -4.8 with therapy. In addition, at week 56, there were no differences in severe HIT-6 scores and changes from baseline in total HIT-6 scores between Botox and placebo.

The most frequently reported adverse effects of Botox after treatment for chronic migraine versus placebo include neck pain (9% for Botox versus 3% with placebo), headache (5% versus 3%), eyelid ptosis (4% versus less than 1%), migraine (4% versus 3%), muscular weakness (4% versus less than 1%), musculoskeletal stiffness (4% versus 1%), bronchitis (3% versus 2%), injection-site pain (3% versus 2%), musculoskeletal pain (3% versus 1%), myalgia (3% versus 1%), facial paresis (2% versus 0%), hypertension (2% versus 1%), and muscle spasms (2% versus 1%).

While we believe new clinical management at Revance is formulating the next therapeutic and aesthetic indications for both RT001 and RT002, the market for an effective topical application is attractive in comparison with the 31 injections of 155 units needed with Botox. However, chronic migraine is historically a difficult area for drug development, with high placebo rates often making clinical development of new classes of therapies difficult.

## RT002: Long-Acting Injectable Could Be Blockbuster in Therapeutic Indications

Following the setbacks observed in the RT001 program, we believe focus may shift toward the RT002 program, which we believe, alone, could be enough to provide significant upside from current share levels. RT002 is the company's injection product designed to provide targeted delivery of botulinum toxin type A to deeper skin layers that RT001 cannot reach, while also reducing unwanted spreading from the site of interest. The company has demonstrated treatment duration of about 7.3 months, or 29.4 weeks, with RT002. We believe that this duration of treatment could provide the biggest added value for the company, as well as the most direct path to taking market share away from currently approved injectable products.

### RT002 Versus Botox Glabellar Lines Direct Comparison Trial Is a Major Event in 2015

On the third-quarter earnings call, management announced the initiation of a Phase II active comparator clinical trial against Botox by the end of the year. Given the head-to-head nature of this trial against the clear market leader, we believe a positive outcome could be enough to drive considerable upside to shares outside of any positive developments from the RT001 program. The design of the trial is a five-arm, dose-ranging study that will include three active arms, a placebo arm, and a comparator arm. The projected enrollment for the multicenter study is 250 patients randomized one-to-one to evaluate safety, efficacy, and duration of effect. The company expects to report interim duration results in late 2015. We believe that if RT002 can show similar efficacy and safety profiles with double the duration (as shown in its previous trials), this product could become a blockbuster and achieve significant market share in both the aesthetic and therapeutic neuromodulator markets.

We believe meaningful differentiation between the injectable products on the market has always been difficult with physicians gravitating to the original neuromodulator and market leader, Botox. Studies comparing the two have not shown clear differences, with a head-to-head comparison between Dysport and Botox published in 2012 finding no major differences in efficacy between the compounds (Yu et al. *Arch Facial Plast Surg*, 2012). We believe that the ability of "me too" neuromodulators, such as Dysport and Xeomin, to capture approximately 24% market share without any significant efficacy, safety, or duration benefits over Botox, suggests a significant opportunity for a differentiated product, such as the long-acting RT002 with potentially twice the duration of all the currently marketed brands.



### Preclinical and Clinical Data to Date Holds Promise for RT002

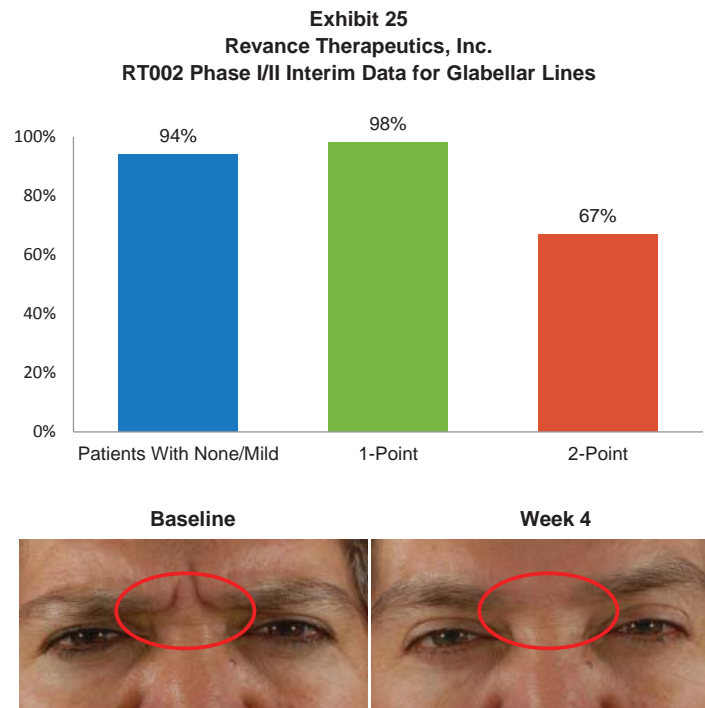
Proof-of-concept animal data was published in 2011 comparing RT002 and Botox in mice for the relative duration of effect for diffusion-matched doses on muscle paralysis (Stone et al. *Toxicon*, 2011). Two groups of mice (n=12 per group) were treated with 1 U/kg of RT002 and Botox and examined at week one following injection. There were no significant differences between RT002 and Botox in both single twitch (p=0.2283) and tetanus (p=0.3782) in percent inhibition of muscle force generation, a measure of efficacy. However, RT002 treatment resulted in a 58%-100% extended duration of effect compared with Botox (exhibit 24).

**Exhibit 24**  
**Maximum Force Generation Recovery Time in Weeks**

% Recovery	RT002		Botox		% Increase in Duration for RT002	
	Single Twitch	Tetanus	Single Twitch	Tetanus	Single Twitch	Tetanus
50%	4.9	1.8	3.1	1.0	58%	80%
75%	12.4	6.1	7.0	3.2	77%	91%
100%	31.6	20.2	15.8	10.5	100%	92%

Source: Stone et al. *Toxicon*, 2011

Subsequent to this data, Revance conducted an open-label Phase I/II dose-escalation study for the indication of glabellar lines consisting of four cohorts to test the safety and efficacy of RT002. Glabellar, or frown, lines are defined as the lines that develop between the eyebrows while frowning. They are most likely to develop in individuals who spend long periods in the sun and occur with aging. As shown in the upper panel of exhibit 25, data from 48 patients at week four indicates the efficacy of RT002 at maximum frown with 94% responders with none or mild glabellar line severity, 98% with a one-point improvement, and 67% with a two-point improvement. In the lower panel of the exhibit is an example of a patient treated with the lowest dose of RT002 at four weeks showing an improvement in glabellar line severity.



Sources: Company reports and William Blair & Company, L.L.C.

Allergan's Botox and Merz's Xeomin have both received approval for the aesthetic benefit in the treatment of glabellar lines; they have been tested to date in about 3,084 and 2,421 patients, respectively. Allergan has conducted two Phase III clinical trials on the temporary improvement of moderate to severe glabellar facial lines. In these trials, subjects received a single treatment of Botox (n=405, combined) or placebo (n=132, combined) with an injection volume of 0.1 mL and four units in five sites for a total of 20 units and five injections. The efficacy results from these studies are shown in exhibit 26. These results show a statistically significant difference from placebo at all the time points tested in both the investigator's assessment and the subject's assessment out to 120 days (about four months). In addition, a subset of subjects equal to or greater than the age of 65 were analyzed and showed a reduced effect in comparison with younger subjects. However, Botox does not report a composite score, whereas both Xeomin and Dysport do.

Exhibit 26				
Botox Efficacy Results for the Indication of Glabellar Lines				
Investigator's Assessment of Glabellar Line Severity at Maximum Frown – Responder Rates (% of Subjects With Severity of None or Mild)				
Day	BOTOX Cosmetic	Placebo	Difference	
7	74%	6%	68%	
30	80%	3%	77%	
60	70%	2%	69%	
90	48%	2%	45%	
120	25%	2%	24%	
Subject's Assessment of Change in Appearance of Glabellar Lines – Responder Rates (% of Subjects With at Least Moderate Improvement)				
Day	BOTOX Cosmetic	Placebo	Difference	
7	82%	9%	73%	
30	89%	7%	83%	
60	82%	4%	78%	
90	63%	3%	60%	
120	39%	1%	38%	
Investigator's and Subject's Assessment – Responder Rates for Subjects <65 Years of Age and ≥65 Years of Age at Day 30				
Assessment	Age Group	BOTOX Cosmetic (N=405)	Placebo (N=132)	Difference
Investigators (max frown)	<65	83%	2%	81%
Subjects	<65	91%	7%	84%
Investigators (max frown)	≥65	39%	22%	17%
Subjects	≥65	70%	11%	58%

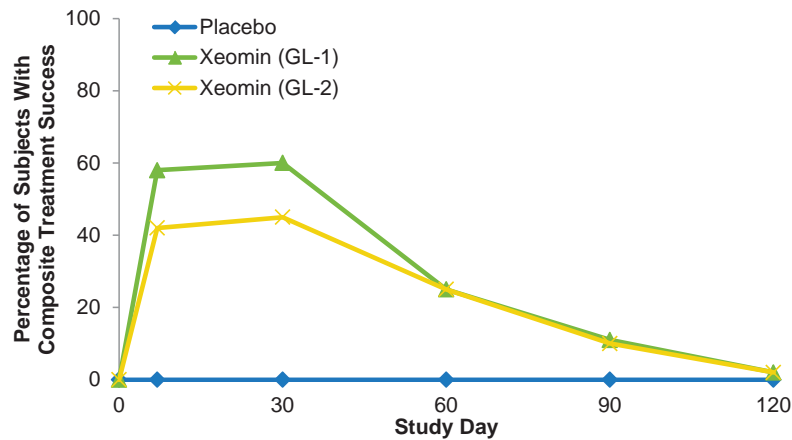
Source: Allergan company reports

Merz's product, Xeomin, has also been examined in two Phase III trials (GL-1 and GL-2) for the indication of temporary improvement of moderate to severe glabellar lines. The studies enrolled 547 subjects; 360 subjects were treated with 20 units of Xeomin at five injection sites (similar to Botox), and 181 subjects were treated with placebo, with a four-point scale used to assess efficacy at maximum frown on day 30. As shown in exhibit 27, Xeomin at day 30 showed a significant increase in composite treatment, as well as in individual investigator and subject assessments. However, Xeomin's length of effect did not extend out to 120 days as with Botox and Dysport (exhibit 28).

**Exhibit 27**
**Xeomin Results for Glabellar Lines – Treatment Success at Day 30\***

	GL-1		GL-2	
	Xeomin (N=184)	Placebo (N=92)	Xeomin (N=184)	Placebo (N=92)
Composite Treatment Success	111	0	87	0
Investigator Assessment	141	0	129	0
Subject Assessment	120	0	101	1

\*At least 2 grades of improvement from baseline at maximum frown  
Source: Merz company reports

**Exhibit 28**
**Duration of Effect After Xeomin Injection in Glabellar Lines**


Source: Merz company reports

As shown in exhibits 29 and 30, although Dysport and Botox cannot be directly compared because the studies were performed in different patients, Dysport has slightly lower efficacy than Botox up to 120 days (according to the Botox data). It can also be seen that the effects of Dysport are reduced to placebo levels by day 150 (or five months). Therefore, the recommendation on the Dysport label is for efficacy up to four months. At day 30, investigator assessment of the percent of subjects with severity of none or mild was 85% for Dysport and 4% for placebo, and subject assessment was 79% for Dysport and 1% for placebo. The numbers are slightly lower than Botox and higher than Xeomin. More importantly, these results are lower than the interim analysis for RT002 (67%), further supporting the idea that the drug could gain significant market share for this indication, if approved.

**Exhibit 29**
**Dysport Combined Subject and Investigator Assessment for Glabellar Lines – Treatment Success at Day 30\***

	2-Grade Improvement	
	Dysport (%)	Placebo (%)
GL-1 (N=158)	55%	0%
GL-2 (N=142)	52%	0%
GL-3 (N=300)	60%	0%

\*At least 2 grades of improvement from baseline at maximum frown  
Source: Dysport label

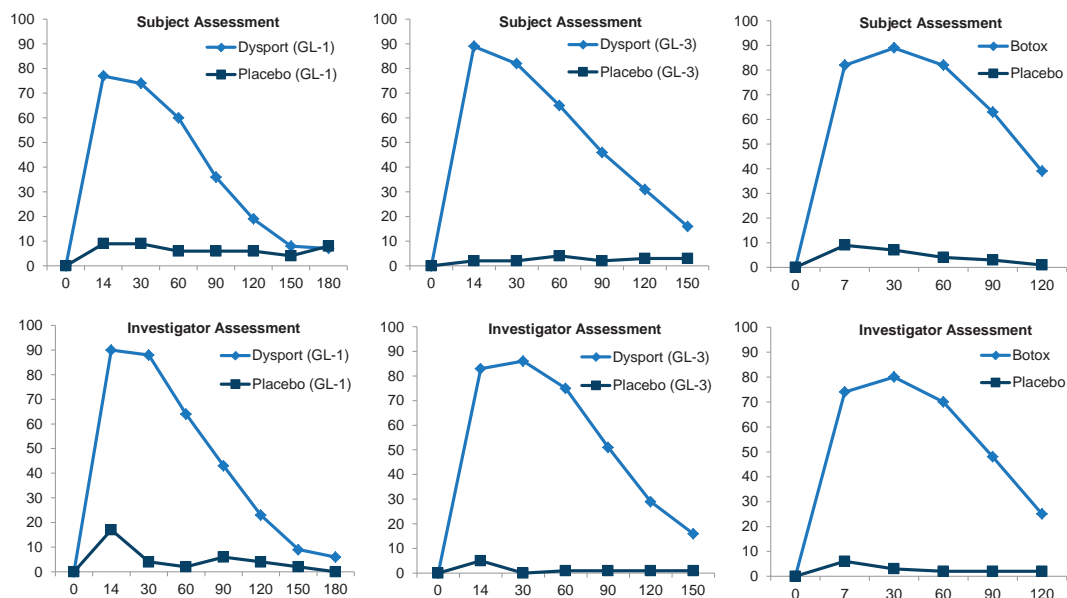
**Exhibit 30**  
**Combined Subject and Investigator Assessment for Glabellar Lines – Treatment Success at Day 30**  
**With at Least 2 Grades of Improvement From Baseline at Maximum Frown**

Product	Study	2-Grade Improvement	Placebo (%)
Dysport	GL-1 (N=158)	55%	0%
	GL-2 (N=142)	52%	0%
	GL-3 (N=300)	60%	0%
Xeomin	GL-1 (N=184)	60%	0%
	GL-2 (N=184)	47%	0%
RT002	Phase I/II (N=48)	67%	N/A

Sources: Company reports and Xeomin/Dysport labels

With the current clinical trial data for RT002 showing about 7.3 months of duration in the Phase I/II trial, we believe that the introduction of this long-acting injectable product could be the greatest value driver for the company. As shown in exhibit 31, using subject assessment and investigator assessment comparisons for Botox and Dysport, the efficacy of both products reaches maximum effect about 14 days after treatment. By day 120, the effects in the subject assessment in both Dysport trials are below 20% of the patient population. Botox seems more efficacious at the 120-day point, with about 39% of subjects seeing a change in appearance. Similar trends are seen in investigator assessments as well. We believe that if Revance can replicate the efficacy data in its Phase II trial and increase the duration of effect from 150 days to over 200 days (or 7.3 months), the potential rollout of RT002 could be disruptive and lead to the investigation of other indications for the product.

**Exhibit 31**  
**Dysport and Botox: Duration of Efficacy in Investigator and Subject Assessments**



Sources: Dysport and Botox labels

The safety profile with Botox injections for glabellar lines (exhibit 32) shows greater than 1% of patients reporting adverse reactions that were attributed to treatment, including facial pain, facial paresthesia, eyelid ptosis, and muscular weakness. Dysport has more adverse events, as shown on the

label; however, as with the comparisons made earlier, it should be noted that these cannot be directly compared. If RT002 can show a similar safety profile, in addition to increased efficacy and duration, it would strengthen the belief that the product could become a blockbuster therapy for the company.

**Exhibit 32**  
**Adverse Reactions Reported by >1% of the BOTOX Cosmetic Treated**  
**Patients and More Frequent Than in Placebo-Treated**  
**Patients in Double-Blind, Placebo-Controlled Clinical Studies of**  
**Treatment of Glabellar Lines**

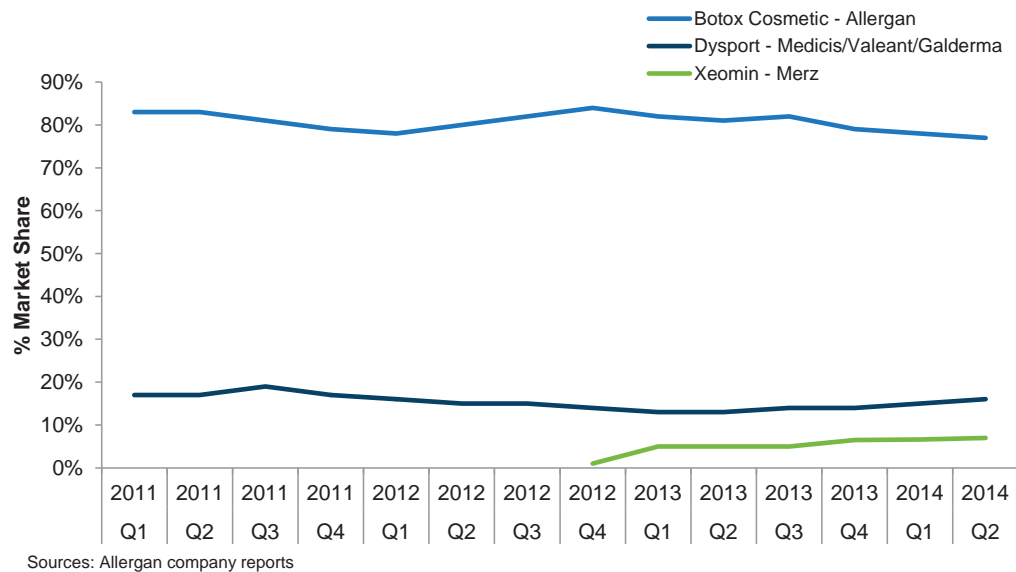
Adverse Reactions by System Organ Class	BOTOX Cosmetic (N=405)	Placebo (N=130)
General Disorders and Administration Site Conditions	6 (1%)	0 (0%)
Facial Pain		
Nervous System Disorders		
Facial Paresis	5 (1%)	0 (0%)
Eye Disorders		
Eyelid Ptosis	13 (3%)	0 (0%)
Musculoskeletal and Connective Tissue Disorders	6 (1%)	0 (0%)
Muscular Weakness		

Source: Allergan company reports

## Competition

As shown in exhibit 33, on the following page, in the U.S. aesthetics market for botulinum toxin products, competition for share is divided primarily among three products: Botox, Dysport, and Xeomin. Botox, marketed by Allergan, is the leader, with about 76% market share as of last quarter. Dysport, with a share of roughly 15%, was approved and launched in 2009 by Medicus, which was subsequently acquired by Valeant and recently sold to Nestlé Skin Health S.A. as part of a package of products for \$1.4 billion. Internationally, Botox has faced competition from neuromodulators produced by Asian and South American sources for several years. We view Merz's Xeomin and Nestlé's Dysport as largely "me too" products in the neuromodulator space, differentiated primarily by marketing, although each product's formulation has slight changes. Previously, we had heard from physicians that the formulation of Dysport has led to an increase in a stinging sensation when patients are injected, although we have also heard similar claims about Botox by physicians loyal to Dysport. In addition, Xeomin's product label claims three months of efficacy, whereas Botox and Dysport are at about four months of efficacy. Even though there is no significant differentiation of Dysport, Xeomin, and biosimilar products from Botox, these products have been able to secure 24% of the market, which is about \$672 million in sales worldwide. We believe that, if approved, RT001 and RT002, with differentiation in delivery method and duration of effect, respectively, could take significant market share from all currently approved products.

Exhibit 33  
U.S. Botulinum Toxin Market for Aesthetics



**The Neuromodulator Market Continues to Grow at a Double-Digit Compound Annual Rate Worldwide**

Over the last several quarters, the worldwide neuromodulator market and the top-10 neuromodulator markets have grown at double-digit rates. Exhibit 34 shows the percent growth on a quarterly basis since 2007, worth an estimated \$2.8 billion worldwide after first quarter 2014 and \$2.1 billion in the top-10 markets. When breaking down the composition of the worldwide Botox market, as in exhibit 35 from Allergan company reports, it can be seen that the trend in the market has been low-double-digit compound annual growth since 2002, and a continuance of growth at that scale based on revenue trends from Botox.

Exhibit 34  
Growth and Total (in billions) Neuromodulator Market

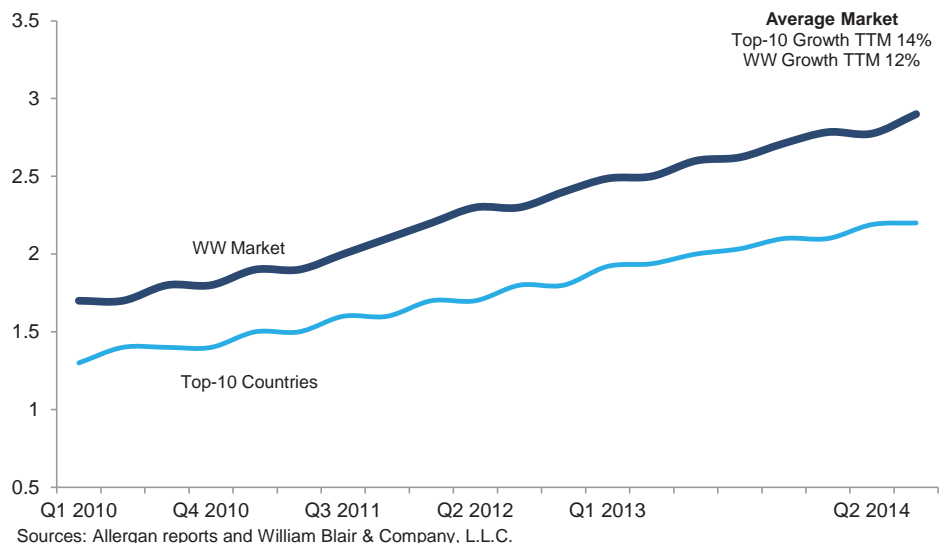
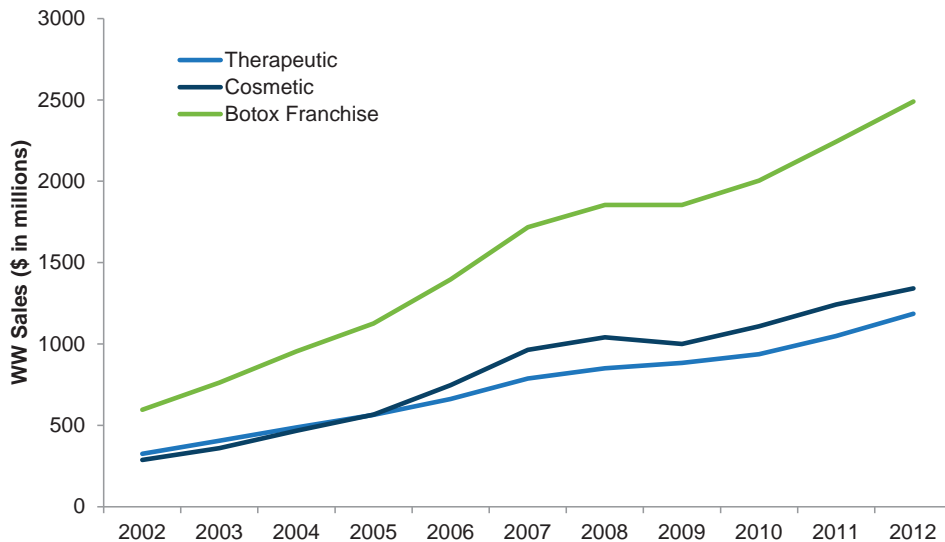




Exhibit 35

## Worldwide Sales of Botox Franchise and Therapeutic/Cosmetic Breakdown (2001-2012)



Source: Allergan company reports

Given the attractiveness of the neuromodulator market, multiple competitors in the space have appeared over the past several years; in general, however, we believe that Revance is developing the most differentiated products in the space with RT001 and RT002. In appendix A, we list the clinical trials completed to date from Revance. Appendix B lists the clinical trials for several competitors of RT001 in several indications, including LCL and hyperhidrosis. Appendix C shows clinical trials performed on glabellar lines, the proposed indication for RT002.

#### Anterios, Inc.

Anterios is a private company that is developing a topical botulinum toxin product called ANT-1207 for wrinkles, hyperhidrosis, and acne and has been analyzed in more than 500 studies to date. The company is in Phase IIb trials, and according to [clinicaltrials.gov](http://clinicaltrials.gov), has three Phase II studies that are establishing safety, tolerance, efficacy, and therapeutic range of the compound. The three studies are enrolling 111, 109, and 145 patients and are using an IGA measurement at two weeks in one study and four weeks in the other two studies to assess efficacy. Self-assessment score up to 12 weeks will be used as a secondary endpoint. In addition, the company announced in March 2014 that it is developing a next-generation injectable product, AI-09, which will be packaged as a ready-to-use injectable liquid, as opposed to currently marketed products that require reconstitution from a powdered form before injection.

#### GFX Nerve Ablation System

The GFX Nerve Ablation System has been cleared via 510(k) by the FDA to create radiofrequency heat lesions in nerve tissue. A clinical trial was enrolled by Advanced Cosmetic Intervention with 94 patients to assess the immediate effectiveness of the GFX device to reduce deep frown lines (glabellar lines) between the eyebrows. The primary endpoint will be a successful result from the GFX procedure in the 7 to 10 days following the procedure. The secondary endpoint revolves around the safety of the treatment; the goal is no major adverse events.

### **PurTox**

PurTox was purchased by Johnson & Johnson from Mentor Worldwide to compete for market share with Botox. According to [clinicaltrials.gov](http://clinicaltrials.gov), Mentor had conducted a Phase III study with 576 patients to evaluate the long-term safety of repeat treatment in glabellar lines. In April 2014, Johnson & Johnson announced that it was ending efforts to develop PurTox, which according to the company was due to the desire to focus on its core breast surgery business.

### **Medical Devices**

Myoscience is a private company that has tested several iterations of its CryoTouch device, a portable cryogenic surgical device that is used to destroy tissue and/or produce lesions in nervous tissue. The company has several clinical trials reported on [clinicaltrials.gov](http://clinicaltrials.gov) for the indication of glabellar lines with endpoints of efficacy and safety measured at 30 days post-treatment using a five-point wrinkle scale. MiraDry is an FDA-cleared procedure using a medical device as a noninvasive procedure for hyperhidrosis. According to the website, MiraDry costs about \$3,000 for two treatments.

### **Medy-Tox**

Allergan and Medy-Tox had previously entered a complete licensing agreement whereby Allergan would pay Medy-Tox an up-front cash payment of \$65 million for exclusive rights to develop (and, if approved, commercialize) certain neurotoxin product candidates, including a potential liquid-injectable product. Allergan also agreed to make contingent milestone payments on development and commercialization up to \$180.5 million. The companies announced the completion of this licensing agreement in January 2014.

### **Generics**

There are a few botulinum toxin type A generics that have been developed, such as Botulax, which was compared with Botox in a Phase III clinical trial in 262 subjects run by Hugel to assess safety and efficacy at 4, 8, 12, and 16 weeks following injection. Another generic equivalent, DWP450, was tested by Daewoong Pharmaceutical and was compared with Botox in a Phase III trial in 268 subjects for safety and efficacy at 4, 8, 12, and 16 weeks. Another trial (Phase II) with DWP450 was run by Evolus to demonstrate the safety of multiple doses of DWP450 for glabellar lines.

## **Management Team**

Revance's management team includes both co-founders, as well as individuals with expertise in clinical development and work experience from Allergan. The TransMTS peptide delivery system was developed by one of the company's co-founders and current chief scientific officer. In addition, the company recently added a new chief medical officer and vice president of quality as it heads toward conducting a strong Phase III clinical program in 2015. We believe the team, after a few setbacks in the second half of 2014, is committed and will be able to move its products through the development and regulatory processes into commercialization.

**L. Daniel Browne, co-founder, president, and chief executive officer.** Mr. Browne has served as president and CEO and member of the board of directors since the company was founded in 2002. Before co-founding Revance, Mr. Browne served as president and CEO of Neomend and president of Prograft Medical. Mr. Browne has a B.S. from the University of Hawaii in cell and molecular biology and an M.B.A. from Pepperdine University.

**Lauren P. Silvernail, chief financial officer and executive vice president of corporate development.** Ms. Silvernail has been with Revance since March 2013. Ms. Silvernail was previously CFO and vice president of corporate development at ISTA Pharmaceuticals. In addition, she has eight years of experience with Allergan, the maker of Botox, in various operating and corporate

development positions, including vice president of business development. Ms. Silvernail has an M.B.A. from the University of California, Los Angeles, and a B.A. in biophysics from the University of California, Berkeley.

**Jacob Waugh, M.D., co-founder, chief scientific officer, and medical director.** Dr. Waugh, the other co-founder of Revance, has served as chief scientific officer and medical director since the company's inception. The TransMTS peptide delivery technology used by the company was developed by Dr. Waugh. Until 2004, Dr. Waugh served on staff at the Stanford University School of Medicine. Dr. Waugh received his M.D. from the Baylor College of Medicine and his B.S. from Rice University.

**Arthur P. Bertolino, M.D., Ph.D., chief medical officer.** Dr. Bertolino is a board-certified dermatologist and veteran industry executive with nearly 30 years of experience. He most recently served as vice president of dermatology for the Novartis Institutes for Biomedical Research (NIBR). Previously, he was the vice president and global head of translational medicine for autoimmunity, immunology, and dermatology at the NIBR. Before Novartis, he worked in senior roles for Peplin, Inc. and Pfizer Inc. Dr. Bertolino received his M.D. and Ph.D. at the Johns Hopkins University School of Medicine and his postgraduate training at NYU School of Medicine. He received his M.B.A. from the Stephen M. Ross School of Business at the University of Michigan.

**Curtis Ruegg, Ph.D., executive vice president, research and development and technical operations.** Dr. Ruegg has been with Revance since September 2006. Previously, Dr. Ruegg held management and R&D positions at CoTherix. From 2002 to 2004, Dr. Ruegg was vice president of preclinical and process development at InterMune and vice president of R&D at AP Cells. Dr. Ruegg obtained his Ph.D. in pharmacology from the Johns Hopkins University School of Medicine and his B.S. in toxicology from the University of California, Davis.

## Financial Overview

### Income Statement

The performance of Revance's shares will largely be dictated in the near term by the development of the company's two main pipeline assets: RT001 is in a Phase III trial for LCL; and RT002 is the company's long-acting botulinum toxin type A product in development for glabellar lines and therapeutic indications. We are not assuming the company will break into profitability until 2019 as the company gains traction with RT001 following a launch anticipated in 2018. We believe that the company will break into profitability in 2019, posting \$0.81 in EPS during the year. Between 2015 and profitability in 2019, we estimate the company will use \$223 million in cash as it advances RT001 and RT002 in clinical development and through the regulatory process and prepares for market entry of RT001 in 2018.

Gross margins for RT001 and RT002 should exceed 80%, although the company's own manufacturing assets, which we view as a significant strategic asset, will likely dampen margins on a noncash basis. As Revance approaches commercialization, we believe that SG&A expense will rise from about \$19 million in 2014 to peak levels of more than \$70 million as the company brings RT001 and RT002 to the market with a relatively concentrated salesforce. With about 17,000 dermatologists in the United States, we believe Revance should be able to use 150 sales representatives at the time of launch of both products, which we assume should cost \$37.5 million to \$40 million in salary alone and build capabilities as the company gains traction in the market. Before commercialization, we expect the company to invest in its late-stage pipeline with consistent R&D spending of \$30 million to \$45 million from 2014 through 2017. Over the longer term, we believe that SG&A expense will be about 20% of product sales, which is in line with the company's specialty peers, while R&D spending will likely moderate significantly pending approval of RT001 in 2018 and RT002 in 2019. We have included our income statement estimates in exhibit 36, on the following page.

**Exhibit 36**  
**Revance Therapeutics, Inc.**  
**Income Statement**  
(\$ in thousands except EPS data)

	2012(A)	2013(A)	Q1(A)	Q2(A)	Q3(A)	Q4(E)	2014(E)	2015(E)	2016(E)	2017(E)	2018(E)	2019(E)	2020(E)
Product Revenue													
RT001 - LCL	-	-	-	-	-	-	-	-	-	-	18,127	81,608	229,627
RT002 - Glabellar Lines	-	-	-	-	-	-	-	-	-	-	-	38,846	126,809
RT002 - Therapeutic	-	-	-	-	-	-	-	-	-	-	-	17,283	54,443
Total Product Revenue	-	-	-	-	-	-	-	-	-	-	18,127	137,738	410,878
Other Revenue	-	-	158.0	75.0	75.0	75.0	383	600	600	600	600	600	600
<b>Total Revenue</b>	<b>717.0</b>	<b>617.0</b>	<b>158.0</b>	<b>75.0</b>	<b>75.0</b>	<b>75.0</b>	<b>383.0</b>	<b>600.0</b>	<b>600.0</b>	<b>600</b>	<b>18,727</b>	<b>138,338</b>	<b>411,478</b>
yr/yr growth	28.7%	-13.9%	110.7%	NA	NA	NA	-37.9%	NM	NM	NM	NM	638.7%	197.4%
q/q growth	NA	NA	NA	NA	NA	NA							
Cost of Goods Sold	-	-	0	0	0	0	-	-	-	75	5,438	15,865	18,974
<b>Gross Profit</b>	<b>717</b>	<b>617</b>	<b>158</b>	<b>75</b>	<b>75</b>	<b>75</b>	<b>383</b>	<b>600</b>	<b>600</b>	<b>525</b>	<b>13,289</b>	<b>122,472</b>	<b>392,504</b>
<b>SG&amp;A</b>	<b>11195</b>	<b>11011</b>	<b>4093</b>	<b>4857</b>	<b>5300</b>	<b>5000</b>	<b>19250</b>	<b>21250</b>	<b>23250</b>	<b>26250</b>	<b>32250</b>	<b>56750</b>	<b>93750</b>
Growth y/y	NA	-2%	-45.6%				20%	10%	9%	13%	23%	76%	65%
<b>R&amp;D</b>	<b>32708</b>	<b>27831</b>	<b>7551</b>	<b>8110</b>	<b>8600</b>	<b>7000</b>	<b>31261</b>	<b>46892</b>	<b>51581</b>	<b>41265</b>	<b>45391</b>	<b>49930</b>	<b>54923</b>
Growth y/y	-15%	239%					12%	50%	10%	-20%	10%	10%	10%
<b>Total Operating Expenses</b>	<b>43,903.0</b>	<b>38,842.0</b>	<b>11,644</b>	<b>12,967</b>	<b>13,900</b>	<b>12,000</b>	<b>50,511.0</b>	<b>52,198.4</b>	<b>57,293.2</b>	<b>67,514.5</b>	<b>77,641</b>	<b>106,680</b>	<b>148,673</b>
Growth y/y	55.16%	-11.53%	19%	NA	NA	NA	30.04%	3.34%	9.76%	17.84%	15.00%	37.40%	39.36%
Operating Income	(43,186)	(38,225)	(11,486)	(12,892)	(13,825)	(11,925)	(50,128)	(51,598)	(56,693)	(66,990)	(58,914)	31,658	262,805
Growth y/y (%)	NA	-11.5%	18.7%	NA	NA	NA	-31.1%	-2.9%	-9.9%	-18.2%	-12%	-154%	-730%
Interest Income	7.0	2.0	2.0	1.0	14.0	1.0	18.0	500	5.0	5.0	5.0	5.0	5.0
Interest Expense	(28,959.0)	(15,164.0)	(9,841)	(267)	(228)	(200)	(10,536)	(200)	(2.0)	(2.0)	(2.0)	(2.0)	(2.0)
Change in fair value of derivative liabilities			3,886	(76)	67	(100)	3,777	(400.0)	(400.0)	(400.0)	(400.0)	(400.0)	(400.0)
Change in fair value of comm/pref stock warrant liabilities			(2,361)	-	-	-	(2,361)	-	-	-	-	-	-
Loss on settlement of preferred stock warrant			(1,356)	-	-	-	(1,356)	-	-	-	-	-	-
Depreciation and Amortization	9,504	6,226	1,557	1,557	1,561	1,557	6,231	6,481	6,731	6,981	7,231	7,481	7,731
EBITDA	(33,682)	(31,999)	(9,930)	(11,336)	(12,264)	(10,369)	(43,898)	(51,598)	(56,693)	(60,009)	(51,684)	39,138	270,536
Other income	13,879.0	939.0	(9,940.0)	(68.0)	(5.0)	(100.0)	(10,113)						
Income Before Taxes	(58,259.0)	(52,448.0)	(21,426.0)	(13,302.0)	(13,977.0)	(12,324.0)	(61,029)	(51,598.4)	(56,693.2)	(66,989.5)	(58,914.0)	31,657.7	262,805.2
Income Tax Provision	-	-	-	-	-	-	-	-	-	-	-	11,396.77	94,609.87
Effective Tax Rate	0%	0%	0.0%	0.0%	0.0%	0.0%	0%	0%	0%	0%	0%	36%	36%
<b>Net Income (loss)</b>	<b>\$(58,259.0)</b>	<b>\$(52,447.9)</b>	<b>(21,426.0)</b>	<b>(13,302.0)</b>	<b>(13,977.0)</b>	<b>(12,324.0)</b>	<b>\$(61,029.0)</b>	<b>\$(51,598.3)</b>	<b>\$(56,693.1)</b>	<b>\$(66,989.5)</b>	<b>\$(58,914.0)</b>	<b>\$20,260.9</b>	<b>\$168,195.3</b>
Net loss per share (fully diluted)	\$ (290.48)	\$ (2.69)	(1.93)	(0.69)	(0.60)	(0.53)	\$ (3.16)	\$ (2.49)	\$ (2.56)	\$ (2.90)	\$ (2.44)	\$ 0.81	\$ 6.44
Basic weighted avg. shares of common out	200,560	19,514	11,092	19,381	23,331	23,431	19,309	23,681	24,081	24,581	25,581	26,581	27,581
Diluted weighted avg. shares of common out	200,560	1,029,150	11,092	19,381	23,331	23,431	19,309	20,709	22,109	23,109	24,109	25,109	26,109
<b>Key Ratios (GAAP unless noted)</b>													
Gross Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	50.0%	70.0%	80.0%	85.0%
R&D (% Total Rev.)	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	242.4%	36.1%	13.3%
SG&A (% Total Rev.)	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	172.2%	41.0%	22.8%
Operating Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	22.9%	63.9%
Net Income Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	14.6%	40.9%
<b>Revenue Growth</b>													
Growth Yr/Yr	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	3021%	639%	197%
<b>SG&amp;A Growth</b>													
Growth Yr/Yr	NM	-2%	NM	NM	NM	NM	75%	10%	9%	13%	23%	76%	65%
<b>R&amp;D Growth</b>													
Growth Yr/Yr	NM	-15%	NM	NM	NM	NM	12%	50%	10%	-20%	10%	10%	10%

Sources: Company reports and William Blair & Company, L.L.C. estimates

### Balance Sheet and Cash Flow

We estimate that Revance holds about \$187.5 million in cash on its balance sheet after third quarter 2014, following a successful public offering earlier in the year when the company priced shares at \$16 and netted \$98.7 million in cash, and a follow-on offering when it priced shares at \$30.50 and netted \$103 million in cash. Although additional nondilutive capital may be available to the company through a partnership outside the United States or in Japan, we would not rule out the possibility of another opportunistic raise following positive Phase III data or additional data from RT002 in late 2015. The company has stated that it has about two years of cash on hand.

Throughout its operating history, Revance has accumulated net losses of \$120 million after what we believe was a longer-than-anticipated development pathway for RT001. We anticipate that Revance will use \$69 million in cash during 2014, which is within the company's guided range of \$65 million to \$75 million. This spending will be heavily influenced by the development of RT001 and RT002.

## Valuation and Stock Thoughts

Shares of Revance have been weak following the release of FDA guidelines for the endpoints to be used in facial aesthetic clinical trials and the company's decision to delay the initiation of its pivotal Phase III trial. The weakness in shares, however, allows for an attractive entry point in a company that we believe holds two unencumbered assets by which proof-of-concept data in either the RT002 glabellar lines Phase II or the RT001 hyperhidrosis Phase II would be significant catalysts for shares. While we believe there is strong reason to anticipate that both programs will be successful, we ultimately believe from current shares prices that only one will be necessary to drive significant upside.

While we understand investor hesitation surrounding RT001 given the recent FDA guidelines and issues with the efficacy observed from the company's own manufactured product, we believe that the potential for a topical botulinum toxin product that perfectly fits physicians' need for a more natural effect is worth the risk; RT002 does not hold the same risk profile surrounding its endpoints and could also prove transformational in the large therapeutic market.

We are establishing a price target of \$35, based on a net present value (NPV) of the company's lead development program, RT001, which we assume in our NPV has a 25% likelihood for success; however, while we believe this to be a conservative view in terms of the efficacy and safety of the product, we believe this also conservatively handicaps the risk surrounding the recent FDA aesthetic guidelines and manufacturing capabilities. On a successful Phase II open-label study using the RT001 manufacturing facilities in early 2015, we would expect to increase this probability of success as the company details its plans for the Phase III program and establishes new timelines for potential NDA and MAA submission/approval.

We also place a higher value on RT002 than RT001, accounting for \$26 in our NPV calculation. While RT002 does not have exposure to the discussions surrounding the appropriate endpoints for facial aesthetic procedures, the product is in an earlier stage of development, which we believe is accounted for in our 40% risk adjustment. We assume peak-year sales of RT001 will reach about \$300 million, and we project RT002 peak-year sales approaching \$700 million, both of which may be conservative given their highly differentiated profiles and the 12% growth in the worldwide neuromodulator market in recent years. Exhibit 37, on the following page, includes our risk-adjusted NPV breakdown for RT001 and RT002.

**Exhibit 37**  
**Revene Therapeutics, Inc.**  
**Risk-Adjusted Sum-of-the-Parts Valuation**

Program	Peak Sales (\$M)	Discount Rate	Probability of Success	Value per share
RT001	\$300	11%	25%	\$ 5.45
RT002	\$650+	11%	40%	\$ 26.09
Cash per share				\$ 8.04
Discounted value of future net loss				\$ (4.54)
<b>Sum-of-the-parts NPV valuation</b>				<b>\$ 35.03</b>

Source: William Blair & Company, L.L.C. estimates

In exhibit 38, we provide the enterprise values of other development companies with either Phase III data in hand or recently approved therapies. We believe the closest comparable is Kythera Biopharmaceuticals, which is developing an aesthetic product for the reduction of submental fat. However, unlike Revene, Kythera lacks an underlying technology platform and additional pipeline assets, so we view the \$779 million in enterprise value as an attractive comparable for Revene, highlighting the opportunity for investors given the recent pullback in shares. Median comparable enterprise values that we include in our comp group suggest a potential enterprise value of \$722 million for late-stage assets, suggesting a 70% discount for Revene to this group alone. Given the significant discount to Kythera and the company's peer group, we believe shares of Revene should trade well as the company executes on its clinical program for RT001 in LCL and hyperhidrosis indications in 2015, the clinical program readouts for RT002 in glabellar lines, and investors become more comfortable with the efficacy and duration of RT001 and RT002.

**Exhibit 38**  
**Comparison Companies**

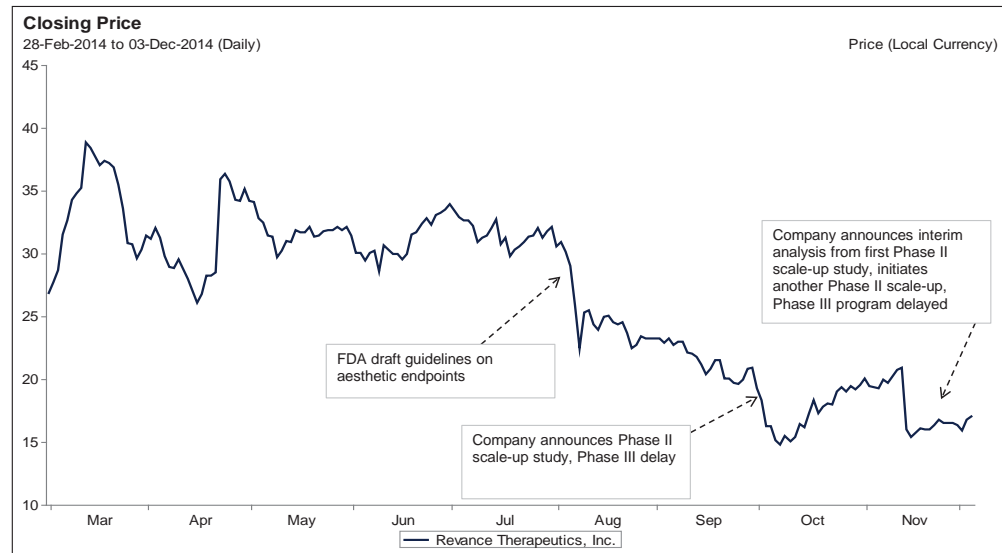
Company	Ticker	Rating	Price Target	Last	Market Cap (in mil.)	Consensus Revenue Estimates		EPS Estimates		Debt	Cash (in mil.)	Enterprise Value (in mil.)
						2014E	2015E	2014E	2015E			
Pacira Pharmaceuticals Inc.	PCRX	Not Rated	N/A	\$93.93	\$3,387	\$196.32	\$330.71	(\$0.41)	\$2.01	\$103	\$152	\$3,338
Anacor Pharmaceuticals, Inc.	ANAC	Not Rated	N/A	\$34.48	\$1,479	\$16.23	\$34.58	(\$2.38)	(\$1.87)	\$29	\$142	\$1,366
GW Pharmaceuticals plc (ADR)	GWPH	Not Rated	N/A	\$77.43	\$1,521	\$51.43	\$67.30	(\$2.04)	(\$3.27)	\$3	\$288	\$1,236
Kythera Biopharmaceuticals, Inc.	KYTH	Not Rated	N/A	\$38.25	\$867	N/A	\$17.31	(\$4.14)	(\$3.70)	\$29	\$117	\$779
Relypsa, Inc.	RLYP	Not Rated	N/A	\$24.89	\$851	N/A	\$8.09	(\$2.44)	(\$3.01)	\$16	\$140	\$728
BioDelivery Sciences International, Inc.	BDSI	Outperform	\$23.00	\$15.35	\$787	\$41.71	\$90.17	(\$1.06)	\$0.04	\$14	\$86	\$716
Auspex Pharmaceuticals, Inc.	ASPX	Outperform	\$42.00	\$24.23	\$668	\$0.00	\$2.35	(\$2.49)	(\$2.05)	\$15	\$159	\$523
Versartis, Inc.	VSAR	Not Rated	N/A	\$18.02	\$436	N/A	N/A	(\$2.97)	(\$2.44)	\$0	\$182	\$254
AcelRx Pharmaceuticals, Inc.	ACRX	Not Rated	N/A	\$6.66	\$291	\$5.06	\$17.57	(\$0.97)	(\$1.08)	\$25	\$86	\$231
<b>Revene</b>	<b>RVNC</b>	<b>Outperform</b>	<b>\$35.00</b>	<b>\$17.42</b>	<b>\$413</b>	<b>N/A</b>	<b>N/A</b>	<b>(\$2.79)</b>	<b>(\$3.57)</b>	<b>\$11</b>	<b>\$188</b>	<b>\$237</b>
Mean												\$938
Median												\$722

Sources: FactSet and William Blair & Company, L.L.C. estimates

### Stock Performance

The performance of Revene shares (shown in exhibit 39) has declined, compared with the S&P 500 increase of 12.1%, the Nasdaq Biotechnology Index increase of 35.2%, and the Russell 2000 increase of 0.8% in 2014 year-to-date. Based on our belief that Revene holds two significantly differentiated assets, RT001 and RT002, we expect shares to outperform the broad market in the next 12 months. In that period, we believe that the company has several clinical catalysts that should drive share performance, including data from the RT001 confirmatory open-label studies, the potential Phase III program of RT001 in LCL, the Phase II study of RT001 in the hyperhidrosis indication, as well as the interim readout of the Phase II comparator study of RT002 and Botox in glabellar lines.

**Exhibit 39**  
**Revance Therapeutics, Inc.**  
**Closing Price Since Feb 28, 2014**



Source: FactSet

## Conclusion

Revance is developing two products—RT001 and RT002—that provide a differentiation in treatment from the currently approved products for LCL and glabellar lines, respectively, as a result of the company’s proprietary TransMTS delivery technology. We believe that a noninvasive botulinum toxin product in RT001 and the longer-duration botulinum toxin RT002 are the most differentiated products to be developed in a space that has seen successful “me too” products. Given its products’ differentiation, we believe Revance could gain significant share in the injectable market because of the need for a less invasive delivery in certain aesthetic areas and the aesthetic benefits (“more natural look”) of RT001; in addition, reducing the frequency of injections is one of the greatest needs we have heard from consulting physicians. While the development of RT001 has experienced several setbacks in recent months, we ultimately view the opportunity for the product in hyperhidrosis as warranting continued clinical development. We also believe the potential for RT002 alone, which holds a blockbuster potential in the \$2.8 billion injectable neurotoxin market, should drive significant upside from current levels pending positive proof-of-concept data during 2015.

We are therefore launching coverage of Revance with an Outperform rating and Aggressive Growth company profile, with our risk-adjusted NPV suggesting a fair value of \$35 per share. Risks to our rating include the recent scrutiny surrounding endpoints in lateral canthal lines, clinical risks that have been highlighted by the recent issues with the RT001 program, and the industrywide risks surrounding development-stage therapeutics companies, which include other regulatory, manufacturing, and market risks.



**Appendix A**  
**Revence Therapeutics, Inc.**  
**Summary of Clinical Trials Completed to Date With RT001**

Condition	Study Type	N	Purpose (from clinicaltrials.gov)	Intervention	Primary Outcome Measure	Secondary Outcome Measure	Completion Date
LCL	Phase II	60	To evaluate the safety and efficacy of RT001 to treat moderate to severe LCL in adults	RT001 (4 doses) v Vehicle Comparator	Improvement via the Investigator Global Assessment at Smile from Baseline (Day 0) to End of Study (Day 28)	The number of subjects classified as exhibiting improvement via the Investigator Global Assessment at Rest from Baseline (Day 0) to End of Study (Day 28) Incidence of treatment-emergent AEs	January-09
LCL	Phase II	30	To determine the safety and efficacy of 2 sequential doses of RT001 compared with vehicle control following applications at baseline (Day 0) and week 2	RT001 (two sequential doses at 0 and week 2) v. Placebo	Improvement via the Investigator Global Assessment from Baseline (Day 0) to End of Study (Week 6)	Incidence of treatment emergent AEs at 6 weeks	April-09
LCL	Phase II	72	To evaluate the safety and efficacy of RT001 to treat moderate to severe LCL in adults and duration of effect	RT001 (2 doses) v Placebo	Improvement via the Investigator Global Assessment at Rest from Day 0 to Day 28	Incidence of treatment-emergent adverse events	October-09
LCL	Phase II	73	To evaluate the efficacy and safety of a single administration of RT001 compared with placebo gel for the treatment of moderate to severe LCL	RT001 (1 dose) v Placebo	Improvement via the Investigator Global Assessment of Lateral Canthal Line Severity at Rest from Baseline (Day 0) to Week 4; incidence of treatment emergent AEs	Primary endpoint from Week 4 and Baseline (Day 0) to Week 6	October-09
LCL	Phase II	36	To evaluate the safety and efficacy of 2 sequential doses of RT001 compared with placebo gel to treat moderate to severe LCL in adults	Botulinum Toxin Type A (two sequential doses at 0 and week 4) v. Placebo	Improvement via the Investigator Global Assessment of Lateral Canthal Line-Rest Severity Scale of the LCA at Baseline compared to Week 8; incidence of treatment emergent AEs	Improvement via the Investigator Global Assessment of Lateral Canthal Line Severity at Smile and at Rest from Baseline to Weeks 2, 4, 6, 8; incidence of treatment emergent AEs	October-09
LCL	Phase II	90	To evaluate RT001 Botulinum Toxin Type A Topical Gel safety and efficacy in lateral canthal lines	Botulinum Toxin Type A (1 dose) v Placebo	Improvement based on the investigator global and patient assessments (4 weeks)	Primary outcome at 8 weeks	July-10
LCL	Phase II	180	To evaluate RT001 Botulinum Toxin Type A Topical Gel safety and efficacy in lateral canthal lines	RT001 (2 doses) v Vehicle v Placebo (4-arm trial)	Subject improvement based on investigator assessment (week 4)	Subject improvement based on patient assessments (week 4)	July-10
LCL	Phase II	40	This study's objective is to evaluate if RT001 is safe and well-tolerated following 2 sequential applications	RT001 (1 dose)	Assessment of treatment-emergent adverse events at 4 weeks and 8 weeks	NA	July-10
LCL	Phase III	247	To evaluate the efficacy and safety of botulinum toxin type A compared with placebo control for the treatment of moderate to severe crow's feet lines (RADIANT)	Botulinum Toxin Type A (1 dose) v Placebo	Composite endpoint based on the investigator global assessment and patient assessment of severity of LCL	2 point or greater improvement from baseline using the IGA 1 point or greater improvement from baseline using the IGA 2 point or greater improvement from baseline using the PSA	May-13
LCL	Phase II	82	This study will confirm the efficacy and safety of a single topical administration of botulinum toxin type A compared with placebo control for the treatment of moderate to severe crow's feet lines	Botulinum Toxin Type A v Placebo	Composite endpoint based on the investigator global assessment and patient assessment of severity of LCL (week 4)	IGA with 2 points or greater improvement from baseline IGA with 1 point or greater improvement from baseline Patient Severity Assessment with 2 points or greater improvement from baseline All at week 4	November-13

Sources: clinicaltrials.gov and William Blair & Company, L.L.C.

**Appendix B**  
**Clinical Trials Completed to Date With Selected Compounds Targeting LCL**

Company	Compound	Condition	Study Type	N	Purpose (from clinicaltrials.gov)	Intervention	Primary Outcome Measure
Anterios, Inc.	ANT-1207	LCL	Phase II	111	To provide evidence of the safety, tolerance, and efficacy of ANT-1207 in the treatment of crow's feet	ANT-1207 (5 doses) v. placebo	Efficacy will be assessed by Investigator's Global Assessment Score (2 weeks)
Anterios, Inc.	ANT-1401	LCL	Phase II	109	To confirm the effect of ANT-1401 in the treatment of LCL	ANT-1401 (2 doses) vs. placebo	Investigator's Global Assessment Scale (4 weeks)
Anterios, Inc.	ANT-1401	LCL	Phase II	145	To establish the therapeutic range of ANT-1401 in the treatment of crow's feet	ANT 1401 (5 doses) vs. placebo	Investigators Global Assessment Scale (4 weeks)
Allergan, Inc.	Botox	LCL	Phase III	446	To evaluate the safety and efficacy of botulinum toxin type A compared with placebo for the treatment of crow's feet lines	OnabotulinumtoxinA (Botox) v. saline	The composite racial wrinkle scale assessment (combined investigator and Subject Facial Wrinkle scales) at Day 30. Responder is defined as a participant with a $\geq 2$ -grade improvement from baseline.
Allergan, Inc.	Botox	LCL	Phase III	300	To evaluate the safety and efficacy of Botox (botulinum toxin type A) compared with placebo for the treatment of crow's feet lines	Botox (2 doses) v. saline	Investigator's Assessment of the Severity of Crow's Feet Lines at Maximum Smile Using the Facial Wrinkle Scale [Time Frame: Day 30]
Allergan, Inc.	Botox	LCL	Phase III	400	To evaluate the safety and efficacy of Botox (botulinum toxin type A) compared with placebo in patients with moderate to severe crow's feet lines	Botox (1 dose: 24 U) v. saline	Investigator's Assessment of Crow's Feet Lines (CFL) Severity at Maximum Smile Using the 4-point Facial Wrinkle Scale (FWS-A) (Day 30)
Galderma	Azzalure	GK	Phase III	335	To assess the efficacy, safety, and duration of effect of Azzalure compared with placebo in the improvement of moderate to severe LCL and repeated treatment in CL with or without GL up to 1 year	Azzalure	The primary criterion for efficacy is the proportion of responders at Week 4 on the severity of Lateral CL "at maximum smile." A positive response (responder) is defined as a grade of 0 or 1 (none or mild), as assessed by the investigator

Sources: clinicaltrials.gov and William Blair & Company, L.L.C.

William Blair & Company, L.L.C.

**Appendix C**  
**Summary of Selected Clinical Trials Completed to Date Targeting Glabellar Lines (GL)**

Company	Compound	Condition	Study Type	N	Purpose (from clinicaltrials.gov)	Intervention	Primary Outcome Measure
Allergan	Botox, Vistabel, Bocouture	GL	Phase IV	224	Evaluate the safety and efficacy of two different types of botulinum toxin type A for the treatment of glabellar frown lines	Vistabel v. Botox v. Bocouture	Number of subjects with a treatment response at day 28 based on the injector's assessment of the severity of glabellar lines at maximum contraction using the Facial Wrinkle Scale
Allergan	Botox	GL	Phase III	207	Observational study assessing patient satisfaction following at least five years of Botox treatment for glabellar lines	Botox	Percentage of participants mostly or very satisfied with their glabellar lines on the Facial Line Satisfaction Questionnaire (approximately 4-28 weeks following last treatment)
Allergan	Botox	GL	NA	727	Postmarketing surveillance study in Korea will evaluate the safety and efficacy of Botox	Botox	Change from baseline in the investigator assessment of glabellar line severity using a 4-point scale up to 4 years
Allergan	Botox, Juvederm, Latisse, Bimatoprost	GL	Phase IV	100	To evaluate patient satisfaction, aesthetic, and psychological impact of combined treatment	Juvederm Ultra XC and/or Juvederm Ultra Plus XC and/or Juvederm Voluma XC injection	The first visit onset of efficacy as measured by physician assessment and subject assessment (14 days)
Allergan	Botox	GL	Phase III	917	Evaluate the safety and efficacy of botulinum toxin type A compared with placebo for the treatment of crow's feet lines and frown lines	44 units (U) botulinum toxin Type A total dose injected. Patients received two treatments 4 months apart.	Percentage of responders based on composite Facial Wrinkle Scale assessment of crow's feet line severity at maximum smile
Allergan	Botox	GL	Phase III	684	Evaluate the safety and efficacy of botulinum toxin type A compared with placebo for the treatment of crow's feet lines and frown lines	Botox (24U and 44U) v. placebo	The investigator assessed the severity of the patient's crow's feet lines at maximum smile using the 4-point Facial Wrinkle Scale
Merz	Xeomin	GL	Phase III	271	To show the superior efficacy of Xeomin over placebo by evaluation of treatment success analyzing the investigator's rating on the Facial Wrinkle Scale and the patient's assessment on a 4-point scale	Xeomin v Placebo	2-point responders at maximum frown (frown as much as possible) at day 30 by investigator's rating on the Facial Wrinkle Scale and the patient's assessment
Merz	Xeomin	GL	Phase III	276	Evaluation of treatment success analyzing the investigator's rating on the Facial Wrinkle Scale and the patient's assessment on a 4-point scale	Xeomin v Placebo	2-point responders at maximum frown (frown as much as possible) at day 30 by investigator's rating on the Facial Wrinkle Scale and the patient's assessment
Merz	NT 201	GL	Phase II	191	To determine the optimal dose of NT 201 in the treatment of glabellar frown lines	NT 201 (3 doses) v Placebo	Percentage of responders at maximum frown at day 30 as assessed by patient's assessment according to 4-point scale; percentage of responders at maximum frown at day 30 as assessed by the investigator according to FWS
Merz	Xeomin	GL	Phase III	796	To investigate the safety and efficacy of Xeomin during repeat dose treatment of glabellar frown lines	Xeomin (20U)	Safety endpoints – investigator's assessment – patient's assessment (assessment at days 30 and >84)
Merz	Xeomin	GL	Phase III	256	To investigate the efficacy and safety of IncobotulinumtoxinA (Xeomin) in the treatment of glabellar frown lines compared with placebo	Xeomin v Placebo	Investigator's assessment according to the Facial Wrinkle Scale and patient's global assessment

Sources: www.clinicaltrials.gov and William Blair & Company, L.L.C.

# **IMPORTANT DISCLOSURES**

William Blair & Company, L.L.C. was a manager or co-manager of a public offering of equity securities within the prior 12 months.

William Blair & Company, L.L.C. is a market maker in the security of this company and may have a long or short position.

William Blair & Company, L.L.C. intends to seek investment banking compensation in the next three months from the subject company covered in this report.

Within the past 12 months William Blair & Company, L.L.C. has provided or is providing investment banking services to or has an investment services relationship with the subject company covered in this report.

Additional information is available upon request.

This report is available in electronic form to registered users via R\*Docs™ at [www.rdocs.com](http://www.rdocs.com) or [www.williamblair.com](http://www.williamblair.com).

Please contact us at +1 800 621 0687 or consult [williamblair.com/Research-and-Insights/Equity-Research/Coverage.aspx](http://williamblair.com/Research-and-Insights/Equity-Research/Coverage.aspx) for all disclosures.

Timothy Lugo attests that 1) all of the views expressed in this research report accurately reflect his personal views about any and all of the securities and companies covered by this report, and 2) no part of his compensation was, is, or will be related, directly or indirectly, to the specific recommendations or views expressed by him in this report. We seek to update our research as appropriate, but various regulations may prohibit us from doing so. Other than certain periodical industry reports, the majority of reports are published at irregular intervals as deemed appropriate by the analyst.

DJIA: 17,900.10  
S&P 500: 2,071.92  
NASDAQ: 1,227.56

The prices of the common stock of other public companies mentioned in this report follow:

AcelRx Pharmaceuticals, Inc.	\$6.37
Allergan, Inc. (Market Perform)	\$213.71
Anacor Pharmaceuticals	\$35.64
Auspex Pharmaceuticals, Inc. (Outperform)	\$24.53
BioDelivery Sciences International, Inc. (Outperform)	\$14.66
GW Pharmaceuticals plc (ADR)	\$74.55
Kythera Biopharmaceuticals	\$38.31
Pacira Pharmaceuticals	\$93.93
Relypsa, Inc.	\$26.39
Valeant Pharmaceuticals International, Inc.	\$144.43
Versartis, Inc.	\$16.98

## **Current Ratings Distribution (as of 11/30/14)**

<b>Coverage Universe</b>	<b>Percent</b>	<b>Inv. Banking Relationships*</b>	<b>Percent</b>
Outperform (Buy)	64%	Outperform (Buy)	16%
Market Perform (Hold)	31%	Market Perform (Hold)	3%
Underperform (Sell)	1%	Underperform (Sell)	0%

\* Percentage of companies in each rating category that are investment banking clients, defined as companies for which William Blair has received compensation for investment banking services within the past 12 months.

The compensation of the research analyst is based on a variety of factors, including performance of his or her stock recommendations; contributions to all of the firm's departments, including asset management, corporate finance, institutional sales, and retail brokerage; firm profitability; and competitive factors.

#### **OTHER IMPORTANT DISCLOSURES**

Stock ratings, price targets, and valuation methodologies: William Blair & Company, L.L.C. uses a three-point system to rate stocks. Individual ratings and price targets (where used) reflect the expected performance of the stock relative to the broader market (generally the S&P 500, unless otherwise indicated) over the next 12 months. The assessment of expected performance is a function of near-, intermediate-, and long-term company fundamentals, industry outlook, confidence in earnings estimates, valuation (and our valuation methodology), and other factors. Outperform (O) – stock expected to outperform the broader market over the next 12 months; Market Perform (M) – stock expected to perform approximately in line with the broader market over the next 12 months; Underperform (U) – stock expected to underperform the broader market over the next 12 months; not rated (NR) – the stock is not currently rated. The valuation methodologies used to determine price targets (where used) include (but are not limited to) price-to-earnings multiple (P/E), relative P/E (compared with the relevant market), P/E-to-growth-rate (PEG) ratio, market capitalization/revenue multiple, enterprise value/EBITDA ratio, discounted cash flow, and others.

Company Profile: The William Blair research philosophy is focused on quality growth companies. Growth companies by their nature tend to be more volatile than the overall stock market. Company profile is a fundamental assessment, over a longer-term horizon, of the business risk of the company relative to the broader William Blair universe. Factors assessed include: 1) durability and strength of franchise (management strength and track record, market leadership, distinctive capabilities); 2) financial profile (earnings growth rate/consistency, cash flow generation, return on investment, balance sheet, accounting); 3) other factors such as sector or industry conditions, economic environment, confidence in long-term growth prospects, etc. Established Growth (E) – Fundamental risk is lower relative to the broader William Blair universe; Core Growth (C) – Fundamental risk is approximately in line with the broader William Blair universe; Aggressive Growth (A) – Fundamental risk is higher relative to the broader William Blair universe.

The ratings, price targets (where used), valuation methodologies, and company profile assessments reflect the opinion of the individual analyst and are subject to change at any time.

Our salespeople, traders, and other professionals may provide oral or written market commentary or trading strategies—to our clients and our trading desks—that are contrary to opinions expressed in this research. Certain outstanding reports may contain discussions or investment opinions relating to securities, financial instruments and/or issuers that are no longer current. Always refer to the most recent report on a company or issuer before making an investment decision. Our asset management and trading desks may make investment decisions that are inconsistent with recommendations or views expressed in this report. We will from time to time have long or short positions in, act as principal in, and buy or sell the securities referred to in this report. Our research is disseminated primarily electronically, and in some instances in printed form. Electronic research is simultaneously available to all clients. This research is for our clients only. No part of this material may be copied or duplicated in any form by any means or redistributed without the prior written consent of William Blair & Company, L.L.C.

This is not in any sense a solicitation or offer of the purchase or sale of securities. The factual statements herein have been taken from sources we believe to be reliable, but such statements are made without any representation as to accuracy or completeness or otherwise. Opinions expressed are our own unless otherwise stated. Prices shown are approximate.

This material is distributed in the United Kingdom and the European Economic Area (EEA) by William Blair International, Ltd., authorized and regulated by the Financial Conduct Authority (FCA), and is only directed at and is only made available to persons falling within articles 19, 38, 47, and 49 of the Financial Services and Markets Act of 2000 (Financial Promotion) Order 2005 (all such persons being referred to as “relevant persons”). This document is intended for persons regarded as professional investors (or equivalent) and is not to be distributed to or passed onto any “retail clients.” No persons other than persons to whom this document is directed should rely on it or its contents or use it as the basis to make an investment decision.

“William Blair” and “R\*Docs” are registered trademarks of William Blair & Company, L.L.C. Copyright 2014, William Blair & Company, L.L.C. All rights reserved.

# Equity Research Directory

John F. O'Toole, Partner Manager and Director of Research +1 312 364 8612

Kyle Harris, CFA, Partner Operations Manager +1 312 364 8230

## CONSUMER

---

**Sharon Zackfia, CFA, Partner** +1 312 364 5386

Group Head–Consumer

*Apparel and Accessories, Leisure, Restaurants*

**Jon Andersen, CFA, Partner** +1 312 364 8697

*Consumer Products*

**Daniel Hofkin** +1 312 364 8965

*Hardlines, Specialty Retail*

**Mark Miller, CFA, Partner** +1 312 364 8498

*E-commerce, Broad Assortment and Hardlines, Health and Beauty*

**Amy Noblin** +1 415 248 2874

*Apparel and Accessories*

## FINANCIAL SERVICES AND TECHNOLOGY

---

**Adam Klauber, CFA** +1 312 364 8232

Co-Group Head–Financial Services and Technology

*Insurance Brokers, Property & Casualty Insurance*

**Robert Napoli, Partner** +1 312 364 8496

Co-Group Head–Financial Services and Technology

*Business Development Companies, Financial Technology, Specialty Finance*

**Christopher Shutler, CFA** +1 312 364 8197

*Asset Management, Financial Technology*

## GLOBAL INDUSTRIAL INFRASTRUCTURE

---

**Nick Heymann** +1 212 237 2740

Co-Group Head–Global Industrial Infrastructure

*Multi-industry*

**Larry De Maria, CFA** +1 212 237 2753

Co-Group Head–Global Industrial Infrastructure

*Capital Goods*

**Nate Brochmann, CFA** +1 312 364 5385

*Commercial Services, Logistics/Transportation*

**Brian Drab, CFA, Partner** +1 312 364 8280

*Filtration and Water Management, Industrial Technology*

**Chase Jacobson** +1 212 237 2748

*Engineered Equipment, Engineering and Construction*

**Ryan Merkel, CFA** +1 312 364 8603

*Commercial Services, Industrial Distribution*

## GLOBAL SERVICES

---

**Brandon Dobell, Partner** +1 312 364 8773

Group Head–Global Services

*Energy Services, Information Services, Marketing Services,*

*Real Estate Services and Technology, Education Services and Technology*

**Timothy McHugh, CFA, Partner** +1 312 364 8229

*Consulting, HR Technology, Information Services, Staffing*

## HEALTHCARE

---

**Ben Andrew, Partner** +1 312 364 8828

Group Head–Healthcare

*Medical Devices*

**Ryan Daniels, CFA, Partner** +1 312 364 8418

*Healthcare Information Technology, Healthcare Services*

**Margaret Kaczor** +1 312 364 8608

*Medical Devices*

**John Kreger, Partner** +1 312 364 8597

*Distribution, Outsourcing, Pharmacy Benefit Management*

**Tim Lugo** +1 415 248 2870

*Therapeutics*

**Amanda Murphy, CFA** +1 312 364 8951

*Diagnostic Services, Life Sciences, Pharmacy Benefit Management*

**Matthew O'Brien** +1 312 364 8582

*Medical Devices*

**John Sonnier, Partner** +1 312 364 8224

*Biotechnology*

**Brian Weinstein, CFA** +1 312 364 8170

*Diagnostic Products*

**Y. Katherine Xu, Ph.D.** +1 212 237 2758

*Biotechnology*

## TECHNOLOGY, MEDIA, AND COMMUNICATIONS

---

**Jason Ader, CFA, Partner** +1 617 235 7519

Co-Group Head–Technology, Media, and Communications

*IT Systems*

**Bhavan Suri, Partner** +1 312 364 5341

Co-Group Head–Technology, Media, and Communications

*IT Services, Software, Software as a Service*

**Jim Breen, CFA** +1 617 235 7513

*Internet Infrastructure and Communication Services*

**Anil Doradla** +1 312 364 8016

*IT Services, Technical Software, Semiconductors and Wireless*

**Justin Furby, CFA** +1 312 364 8201

*Software as a Service*

**Jonathan Ho** +1 312 364 8276

*Cybersecurity, Security Technology*

**Dmitry Netis** +1 212 237 2714

*Communications Equipment*

**Ralph Schackart III, CFA, Partner** +1 312 364 8753

*Digital Media, Internet*

## EDITORIAL

---

**Steve Goldsmith, Head Editor** +1 312 364 8540

**Jane Beck** +1 312 364 8067

**Beth Pekol Porto** +1 312 364 8924

**Kelsey Swanekamp** +1 312 364 8174

**Lisa Zurcher** +44 20 7868 4549

*William Blair*