vTv Therapeutics Inc.
Form 10-K
March 04, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2015

Or

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission file number: 001-37524

vTv Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware	47-3916571
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
4170 Mendenhall Oaks Pkwy	
High Point, NC	27265
(Address of principal executive offices)	(Zip Code)

(336) 841-0300

(Registrant's telephone number, including area code)

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

Title of each Class	Name of each exchange on which registered
Class A Common Stock (Par Value $0.01)	NASDAQ Global Market

Securities registered pursuant to Section 12(g) of the Act: None

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

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes o No x

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

Indicate by check mark whether the Registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit and post such files). Yes x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

Large accelerated filer o	Accelerated filer o
Non-accelerated filer x (Do not check if a smaller reporting company)	Smaller reporting company o

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

The registrant was not a public company as of the last business day of its most recently completed second fiscal quarter and, therefore, cannot calculate the aggregate market value of its voting and non-voting common equity held by non-affiliates as of such date.

Indicate the number of shares outstanding of each of the Registrant’s classes of common stock, as of March 4, 2016.

Class of Stock	Shares Outstanding
Class A common stock, par value $0.01 per share	9,274,634
Class B common stock, par value $0.01 per share	23,537,866

DOCUMENTS INCORPORATED BY REFERENCE

The information required by Part III (Items 10, 11, 12, 13 and 14) of this form 10-K, to the extent not set forth herein, is incorporated

herein by reference to the Registrant's definitive Proxy Statement for the 2016 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission no later than 120 days after December 31, 2015.

vTv THERAPEUTICS INC. AND SUBSIDIARIES

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FOR THE FISCAL YEAR ENDED DECEMBER 31, 2015

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

As used in this Annual Report on Form 10-K, the "Company", the "Registrant", "we" or "us" refer to vTv Therapeutics Inc., "vTv LLC" refers to vTv Therapeutics LLC, "vTvx Holdings I" or "TTP" refer to vTvx Holdings I LLC (formerly known as TransTech Pharma, LLC), "vTvx Holdings II" or "HPP" refer to vTvx Holdings II LLC (formerly known as High Point Pharmaceuticals, LLC) and "vTv Therapeutics Holdings" refers to vTv Therapeutics Holdings LLC. The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes that appear elsewhere in this report. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates, assumptions and beliefs. Our actual results could differ materially from those discussed in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this report under "Part I—Item 1A, Risk Factors." Forward-looking statements include information concerning our possible or assumed future results of operations, business strategies and operations, financing plans, potential growth opportunities, potential market opportunities, , potential results of our drug development efforts or trials, and the effects of competition. Forward-looking statements include all statements that are not historical facts and can be identified by terms such as "anticipates," "believes," "could," "seeks," "estimates," "expects," "intends," "may," "plans," "pote "predicts," "projects," "should," "will," "would" or similar expressions and the negatives of those terms. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our management's plans, estimates, assumptions and beliefs only as of the date of this report. Except as required by law, we assume no obligation to update these forward-looking statements publicly or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

PART I

ITEM 1. BUSINESS

Overview

We are a clinical-stage biopharmaceutical company engaged in the discovery and development of orally administered small molecule drug candidates to fill significant unmet medical needs. We have a powerful pipeline of clinical drug candidates, led by our programs for the treatment of Alzheimer's disease ("AD") and type 2 diabetes. Our drug candidate for the treatment of AD, azeliragon (TTP488), is an orally administered, small molecule antagonist targeting the receptor for advanced glycation endproducts ("RAGE"), for which we have commenced patient enrollment in a Phase 3 clinical trial (the "STEADFAST Study") under a Food and Drug Administration ("FDA") agreed Special Protocol Assessment ("SPA"). Our type 2 diabetes drug candidates include TTP399, an orally administered, liver-selective glucokinase activator ("GKA"), for which we have completed enrollment in our Phase 2b clinical trial (the "AGATA Study"), and TTP273, an orally administered, non-peptide agonist that targets the glucagon-like peptide-1 receptor ("GLP-1r"), for which we began enrollment in a Phase 2 clinical trial earlier this year. We have three additional programs in various stages of clinical development for the prevention of muscle weakness and the treatment of inflammatory disorders.

Azeliragon and the Treatment of Alzheimer's Disease

Alzheimer's disease is a progressive neurodegenerative disorder that slowly destroys memory and thinking skills, with a number of other behavioral and neuropsychiatric symptoms.

Azeliragon is an orally administered, small molecule drug candidate that has the potential to be among the first FDA approved disease-modifying AD therapeutics due to its novel mechanism of action of inhibiting RAGE. Because of that potential, azeliragon has been awarded Fast Track designation by the FDA. The FDA grants Fast Track designation to facilitate the development and expedite the review of drugs intended to treat serious diseases or conditions and fill an unmet medical need. RAGE is a cell surface receptor that is implicated in many of the processes thought to play a primary role in the development and progression of AD, including amyloid-beta ("A ") transport into the brain, the phosphorylation of tau protein, chronic inflammation, vascular dysfunction, metabolic dysregulation and neurotoxicity. By inhibiting RAGE, azeliragon has the potential to slow the progression of cognitive decline in mild and mild-to-moderate AD patients. We are not aware of any other clinical-stage drugs targeting RAGE. Unlike development stage disease-modifying treatments from other companies that target a singular cause of AD, azeliragon is designed to interact with multiple aspects of AD etiology.

We are currently enrolling the 800-patient STEADFAST Study, a Phase 3 clinical trial, under an FDA-agreed SPA. The STEADFAST Study includes two sub-studies under one protocol (sub-study A and sub-study B). Each sub-study will enroll 400 patients with mild AD, randomized to receive a 5 mg/day dose of azeliragon or placebo on a one-to-one basis, and is powered to achieve statistical significance on the co-primary endpoints—change from baseline in ADAS-COG_{11} and CDR-SB scores, which are standard measures of cognitive impairment and global function in AD patients. Our Phase 2b study of azeliragon in 399 mild-to-moderate AD patients demonstrated a statistically significant benefit at the 5 mg/day dose versus placebo at 18 months with respect to

ADAS-COG$_{11}$ and a post-hoc analysis showed statistically significant lower frequency of psychiatric adverse events. At the same dose, we identified an even more pronounced benefit in ADAS-COG$_{11}$ and CDR-SB scores in an analysis of the sub-population of patients with mild AD. In all of our Phase 1 and 2 clinical trials, azeliragon has been shown to be generally safe and well tolerated at a dose of 5 mg/day. We expect to report topline data from sub-study A of the STEADFAST Study in late 2017/early 2018 and from sub-study B in the second half of 2018. If results from sub-study A are favorable, we plan to initiate discussions with the FDA regarding a new drug application ("NDA") for azeliragon in early 2018 and submit the NDA later in 2018.

TTP399 and TTP273 and the Treatment of Diabetes

Diabetes is characterized by the body's inability to properly use or produce insulin, the hormone necessary for the uptake of sugar from the bloodstream so that it may be converted into energy. Type 2 diabetes is an inability to properly use insulin to control sugar in the bloodstream, and 90 to 95% of diabetes patients have type 2 diabetes. There are multiple drug classes approved for the treatment of type 2 diabetes, including insulin replacement, metformin, sulfonylureas, thiazolidinedione, SGLT-2 inhibitors, DPP-4 inhibitors and injectable GLP-1r agonists. We expect our type 2 diabetes drug candidates to compete in the non-insulin segment of the market. Despite the availability of these drugs, a substantial portion of type 2 diabetes patients are unable to maintain adequate control of blood glucose levels and eventually progress to insulin therapy, demonstrating the need for additional therapies with novel mechanisms of action and routes of administration to improve efficacy and patient compliance.

We are currently evaluating our GKA drug candidate, TTP399, in a 180-patient Phase 2b trial, the AGATA Study, to assess its ability to improve control of blood glucose levels over a six-month period. The primary endpoint of the AGATA Study is the change from baseline in glycosylated hemoglobin ("HbA$_{1c}$") levels. The study has completed enrollment and we expect to report topline data in mid-2016. TTP399 is an orally administered, small molecule, liver-selective GKA, which uses a novel mechanism of action for the treatment of type 2 diabetes. Liver-selective activation of glucokinase ("GK") provides intensive glycemic control without inducing hypoglycemia. Treatment with TTP399 is designed to avoid the safety and tolerability issues that have been associated with other GKA candidate drugs. We completed a six-week Phase 2a clinical trial of TTP399 in 120 type 2 diabetes patients whose glycemic parameters were not well-controlled on metformin, in which patients treated with TTP399 showed statistically significant, dose proportional reductions in HbA$_{1c}$ levels compared with placebo without induction of hypoglycemia, hyperlipidemia or insulin secretion. If approved, we believe TTP399 will compete primarily with oral anti-diabetic drugs ("OADs"), including DPP-4 and SGLT-2 inhibitors. Further, we believe that TTP399 has the potential to demonstrate higher efficacy than competing non-insulin products, the potential to normalize HbA$_{1c}$ levels, and the potential for no contraindication for renal impairment and no risk of pancreatitis. We believe that TTP399 has the potential to be a first-in-class OAD due to its liver-selectivity and novel mechanism of action.

We commenced a Phase 2 clinical trial for our orally administered GLP-1r agonist drug candidate, TTP273, in early 2016, and expect to report topline data in late 2016. TTP273 is a small molecule, non-peptide GLP-1r agonist. Currently available GLP-1r agonists (which are injectable peptides) are well established in terms of efficacy, including the ability to lower blood glucose, decrease HbA$_{1c}$ levels and induce weight loss, but their use has been limited due to their subcutaneous administration and gastrointestinal side effects, including nausea and vomiting. We believe that an orally administered GLP-1r agonist that has the metabolic effects of currently available GLP-1r agonists, without the gastrointestinal side effects typical of this class of compounds, would offer a competitive advantage compared to GLP-1r targeted treatment options currently available. We previously conducted a proof-of-concept study with a first-generation GLP-1r agonist that demonstrated the proof-of-concept for an orally delivered, small molecule GLP-1r agonist with efficacy consistent with marketed GLP-1r agonists. Additionally, we have conducted Phase 1 clinical trials for TTP273 in healthy volunteers and type 2 diabetics that showed that TTP273 was safe and well-tolerated. Our trials have indicated that TTP273 may have superior tolerability compared to competing products and no risk of antibody formation because TTP273 is a small molecule. For these reasons, we believe TTP273 has the potential to expand the market of GLP-1r agonist therapies and replace a number of current GLP-1-related therapies, including DPP-4 inhibitors and injectable GLP-1 analogues.

Other Clinical Programs

We have additional programs in various stages of clinical development for the prevention of muscle weakness and the treatment of inflammatory disorders. For these programs under active development, we plan to continue to evaluate opportunities for furthering their development. Such development many be done internally or through partnering relationships. In addition, we have other pre-clinical and clinical programs that are not currently under active development, and we may decide to further develop or to license one or more of these other programs in the future.

Our Pipeline

We discovered our drug candidates using our proprietary drug discovery platform, TTP Translational Technology. The following table summarizes our current drug candidates and their respective stages of development:

Each of our most advanced drug candidates is the subject of patent and patent applications for composition of matter and method of use in major markets worldwide. Our patents in the U.S. are expected to provide us with intellectual property protection through 2029 for azeliragon, 2030 for TTP399 and 2034 for TTP273, in each case, assuming we obtain the maximum possible extensions.

Our Strategy

Our goal is to leverage our powerful pipeline of orally administered, small molecule drug candidates to deliver novel, differentiated therapies to fill significant unmet medical needs. As key components of our strategy, we intend to:

- Continue Phase 3 enrollment and seek regulatory approval of azeliragon as a disease-modifying treatment for patients with mild AD. We initiated the STEADFAST Study in April 2015 after receiving positive results from an analysis of data collected in our Phase 2b clinical trial of azeliragon in mild-to-moderate AD patients. The STEADFAST Study is being conducted under an FDA-agreed SPA and will serve as a registration trial for regulatory approval in the United States. We expect to report topline data from sub-study A of the STEADFAST Study in late 2017/early 2018 and from sub-study B in the second half of 2018. If results from sub-study A are favorable, we plan to initiate discussions with the FDA regarding an NDA for azeliragon in early 2018 and submit the NDA later in 2018. Additionally, the FDA granted Fast Track designation to azeliragon based on its potential as a disease-modifying therapy.
- Complete Phase 2 development of our type 2 diabetes programs. We are advancing both TTP399 and TTP273 into Phase 2 clinical trials. We recently completed enrollment in the Phase 2b AGATA Study for TTP399, our small molecule liver-selective GKA, and expect topline data in mid-2016. We commenced a three month Phase 2 clinical trial for TTP273, our orally administered GLP-1r agonist, in January 2016 with topline data expected in late 2016. We believe both compounds have the ability to establish significant market share in the type 2 diabetes market.
- Evaluate strategic collaborations for the commercialization of azeliragon. We plan to seek strategic collaborations for the commercialization of and marketing of azeliragon in the United States and the rest of the world.
- Seek strategic collaborations for Phase 3 development and commercialization of our type 2 diabetes programs. We plan to seek strategic collaborations for the development, commercialization of, and marketing of our type 2 diabetes programs, TTP399 and TTP273, in the United States and the rest of the world.
- Continue development of additional pipeline programs and seek strategic development partners for those programs. We intend to continue developing our other drug candidates, while simultaneously evaluating strategic collaborations as they may arise.
- Evaluate opportunities to leverage our TTP Translational Technology to discover additional drug candidates for internal or external development. We will evaluate opportunities to use TTP Translational Technology, our proprietary drug discovery platform, to discover innovative new drug candidates for internal development or to license to third parties, similar to our arrangement with Calithera.

Our Alzheimer's Program – Azeliragon

Azeliragon Overview

Azeliragon is a novel small molecule designed to target RAGE, which we believe is a key upstream factor responsible for disease progression in AD patients. We are currently enrolling patients in the STEADFAST Study, a Phase 3 clinical trial for azeliragon, which is subject to an FDA-agreed SPA. Azeliragon has also received Fast Track designation from the FDA. Results from our Phase 2b study of azeliragon demonstrated a statistically significant and clinically meaningful slowing of cognitive decline over 18 months at the 5 mg/day dose. Due to azeliragon's novel mechanistic properties, we believe that it has the potential to provide a disease-modifying benefit to AD patients.

Alzheimer's Disease Market Opportunity

AD is a progressive neurodegenerative disorder that slowly destroys memory and thinking skills, and eventually the ability to carry out simple tasks. Its symptoms include cognitive dysfunction, memory abnormalities, progressive impairment in activities of daily living and a host of behavioral and neuropsychiatric symptoms. The exact cause of AD is unknown, however, genetic and environmental factors are established contributors. A plaques and neurofibrillary tangles of tau protein in the brain are believed to be the main causes of the disease, leading to loss of neuronal connectivity in the brain. There are currently no cures or disease-modifying therapies for AD, as existing agents ease the symptoms of AD but do not address the underlying causes.

Generally Accepted Alzheimer's Disease Clinical Measurement Scales

The following are commonly used measures for assessing the behavior, function and cognitive impairment of AD patients:

- ADAS-COG$_{11}$. The Alzheimer's Disease Assessment Scale-Cognitive Subscale ("ADAS-COG$_{11}$") test is one of the most frequently used tests to measure cognition in clinical trials. The ADAS-COG$_{11}$ consists of a 70 point scale measured through 11 parts where a higher score indicates more cognitive impairment. A normal score for someone who does not have AD or another type of dementia is five, according to research conducted in 2004 and published in the journal Alzheimer's Disease and Associated Disorders.
- CDR-SB. The Clinical Dementia Rating Scale Sum of Boxes ("CDR-SB") score (range 0 to 18) is obtained by summing ratings in each of six cognitive domains or boxes including memory, orientation, judgment/problem solving, community affairs, home and hobbies and personal care. Higher scores reflect more global impairment.
- MMSE. The Mini-Mental State Examination ("MMSE") is a sensitive and clinically validated 30-point questionnaire that is often used to measure cognitive impairment. Any score greater than or equal to 27 points (out of 30) indicates normal cognition. Below this, scores can indicate severe (≤15 points), moderate (16–20 points) or mild (21–26 points) AD.
- ADCS-ADL. The Alzheimer's Disease Cooperative Study Activities of Daily Living ("ADCS-ADL") is designed to assess mild-to-moderate AD, using activities of daily living, such as reading books or magazines, pastime activities or household chores. The scores range from 0 to 78, with higher scores indicating a greater level of function.
- NPI. The Neuropsychiatric Inventory ("NPI") is a measurement of AD patients' behavior. It is based on a 144 point scale, where a higher score indicates more behavioral impairment.

Current Treatments for Alzheimer's Disease and Their Limitations

Currently, there are no disease-modifying treatments approved for the treatment of AD, and there are only two classes of approved therapies for the treatment of symptoms of AD: acetylcholinesterase inhibitors ("AChEIs") and glutamatergic modulators. AChEIs are designed to slow the degradation of acetylcholine, helping to preserve neuronal communication and function temporarily, but do not slow or halt neuronal death. Glutamatergic modulators are

designed to block sustained, low-level activation of the N-methyl-D-aspartate ("NMDA") receptor without inhibiting the normal function of the receptor in memory and cognition, providing temporary symptomatic relief.

The currently available treatments combat the symptoms of AD rather than the underlying cause, or etiology, and as a result, AD continues to progress in these patients despite treatment. Similarly, the use of antidepressants and antipsychotics are often prescribed off-label to treat the symptoms of severe AD when patients suffer from agitation, aggressive behaviors, psychosis and depression. Recent drug candidates under development include those focused on A synthesis or clearance from the brain, the phosphorylation of tau protein, chronic inflammation, vascular dysfunction, metabolic dysregulation and neurotoxicity.

The Role of RAGE in the Onset of Alzheimer's Disease

RAGE is an immunoglobulin-like cell surface receptor that is overexpressed in brain tissues of patients with AD. We believe that RAGE is an important cellular cofactor that binds ligands that are implicated in multiple etiologies of AD, including A transport into the brain, the phosphorylation of tau, chronic inflammation, vascular dysfunction, metabolic dysregulation and neurotoxicity. These effects are attenuated following antagonism of the RAGE receptor.

Post-mortem studies in AD patients reveal increased RAGE expression in neuronal, microglial and endothelial cells when compared to similar subjects without AD. Cells around senile plaques express higher levels of RAGE during disease progression. Furthermore, expressed levels of RAGE are correlated with the severity of the disease. The data observed in human AD patients is consistent with the multiple pre-clinical in-vitro and in-vivo animal models studied by third parties that show RAGE is overexpressed in brain tissue of AD subjects. Taken together, we believe that literature provides substantial support for RAGE inhibition as a validated and promising therapeutic approach in the treatment of AD.

Our Solution: Azeliragon

Azeliragon is an orally administered, small molecule drug candidate that has the potential to be among the first FDA approved disease-modifying AD therapeutics due to its novel mechanism of action of inhibiting RAGE. We have demonstrated that azeliragon is a potent and selective inhibitor of RAGE and, in an analysis of data collected in our Phase 2b clinical trial, azeliragon slowed the progression of cognitive decline in mild and mild-to-moderate AD patients. Azeliragon has the potential to offer a novel modality in AD therapeutics, and we are not aware of any other clinical-stage drugs targeting RAGE. Because there are currently no approved disease-modifying treatments for AD and since currently approved treatments are focused on symptom relief, we believe that azeliragon represents a new approach for the treatment of AD. In addition, we believe that in order to successfully treat and combat the physiological progression of AD, a disease-modifying therapeutic must act on multiple causes, or etiologies, of the disease. Unlike development stage disease-modifying treatments that target a singular cause of AD, azeliragon is designed to inhibit RAGE, which affects multiple aspects of AD etiology, including A transport into the brain, the phosphorylation of tau, chronic inflammation, vascular dysfunction, metabolic dysregulation and neurotoxicity.

Azeliragon Clinical and Regulatory Overview

We are currently enrolling the 800-patient STEADFAST Study, a Phase 3 clinical trial, under an FDA-agreed SPA. The STEADFAST Study includes two sub-studies under one protocol (sub-study A and sub-study B). Each sub-study will enroll 400 patients with mild AD, randomized to receive a 5 mg/day dose of azeliragon or a placebo on a one-to-one basis, and is powered to

achieve statistical significance on the co-primary endpoints, with topline data expected in late 2017/early 2018 from sub-study A of the STEADFAST Study and in the second half of 2018 from sub-study B of the STEADFAST Study. In accordance with the SPA, we expect to be able to file for regulatory approval of azeliragon following successful completion of this pivotal trial. Azeliragon has been granted Fast Track designation by the FDA.

Our Phase 2b clinical trial in mild-to-moderate AD patients showed a statistically significant improvement in its primary endpoint, change from baseline in ADAS-COG_{11} for the 5 mg/day dose of azeliragon compared with the placebo arm. While the study was not powered to show statistical significance in secondary endpoints, the results also showed improvement in global, functional, behavioral and cognitive secondary endpoints for the 5 mg/day dose of azeliragon compared with the placebo arm, though these improvements were not statistically significant. Furthermore, an analysis found azeliragon to have greater efficacy in the sub-group of mild AD patients, and it is this population that we are studying in our ongoing Phase 3 registration trial. We have completed six Phase 1 and three Phase 2 clinical trials (two enrolling patients with AD and one enrolling patients with diabetic nephropathy) of azeliragon, in which azeliragon has been generally safe and well tolerated at the 5 mg/day dose.

The table below sets forth information regarding our ongoing and completed clinical trials of azeliragon.

Study	Phase	Objectives	Completion Date
STEADFAST	Phase 3	Efficacy in mild AD for 18 months	Est. late-2017/early 2018 and the second half of 2018
TTP488-203	Phase 2b	Safety and efficacy in mild-to-moderate AD for 18 months	December 2010
TTP488-202	Phase 2a	Safety and efficacy in type 2 diabetics with albuminuria	August 2009
TTP488-201	Phase 2a	Safety and efficacy in mild-to-moderate AD for 10 weeks	June 2006
TTP488-106	Phase 1	Evaluate pharmacokinetics (“PK”) and its metabolites in plasma, urine and bile	February 2015
TTP488-105	Phase 1	Evaluation of food effect on commercial formulation	July 2014
TTP488-104	Phase 1	Assess concentration in cerebrospinal fluid (“CSF”)	March 2006
TTP488-103	Phase 1	Assess concentration in CSF	October 2005
TTP488-102	Phase 1	Dose escalation in elderly for safety, tolerability and PK	August 2005
TTP488-101	Phase 1	Dose escalation for safety and PK	November 2004

Ongoing Phase 3 STEADFAST Study

We initiated our Phase 3 clinical trial, the STEADFAST Study, in April 2015 pursuant to an SPA with the FDA. The STEADFAST Study is a randomized, double-blind, parallel group, 18-month trial in patients with mild AD, which is the population that showed greater benefit from azeliragon in an analysis of our Phase 2b trial, on standard of care of AChEIs and/or memantine. For the purposes of the STEADFAST Study, patients with a MMSE score of 21 to 26 are considered to have mild AD. The study is conducted under a single protocol and will enroll 800 patients in total, divided equally across two independent 400-patient sub-studies, in which each subject will receive either a 5 mg/day dose of azeliragon or placebo, randomized on a one-to-one basis, added to the standard of care. The sub-studies are independently powered to demonstrate statistically significant differences in co-primary endpoints at month 18. The STEADFAST Study, if successful, will serve as the basis for filing an NDA in the United States and may also serve as a pivotal trial for marketing applications in other jurisdictions.

The co-primary endpoints for the STEADFAST Study, the change from baseline in ADAS-COG_{11} and CDR-SB scores, are designed to establish efficacy by demonstrating a slowing in the loss of cognition and function in AD patients treated with azeliragon. We are evaluating multiple secondary endpoints and the key secondary endpoint is MRI brain volumetric measures. We believe that MRI imaging for volumetric measures has the potential to demonstrate modification of the underlying disease by azeliragon. Topline results from the STEADFAST Study are expected from sub-study A in late 2017/early 2018 and from sub-study B in the second half of 2018. If results from sub-study A are favorable, we plan to initiate discussions with the FDA regarding an NDA for azeliragon in early 2018 and submit the NDA later in 2018.

Completed Phase 2b Trial (TTP488-203)

Efficacy in Mild-to-Moderate AD Patients

Our completed Phase 2b clinical trial of azeliragon, TTP488-203, was a randomized, double blind, placebo-controlled, 18-month trial assessing the safety and efficacy of azeliragon in 399 patients with mild-to-moderate AD, the intent-to-treat (“ITT”) population. Azeliragon or placebo was added to the standard of care, AChEIs and/or memantine. Patients were randomized to receive an oral dose of 20 mg/day of azeliragon, 5 mg/day of azeliragon or placebo. Patients in the high dose azeliragon arm initially received 60 mg/day of azeliragon for six days followed by a daily 20 mg dose, while patients in the low dose arm initially received 15 mg/day

of azeliragon for six days followed by a 5 mg/day dose. The study was done in partnership with Pfizer and the Alzheimer's Disease Cooperative Study ("ADCS").

The primary endpoint of the study was to impede the progression of AD over 18 months as measured by the change from baseline in ADAS-COG_{11} score. The secondary endpoints included the changes in global, functional, cognitive and behavioral attributes as measured by CDR-SB, ADCS-ADL, MMSE and NPI.

Azeliragon, at the 5 mg/day dose, met its pre-specified ADAS-COG_{11} endpoint demonstrating a statistically significant 3.1 point difference ($p = 0.008$) versus placebo at 18 months in patients with mild-to-moderate AD. The results of the primary ADAS-COG_{11} endpoint are summarized in the figure below.

The analysis presented utilizes the analysis of covariance, or ANCOVA, to determine statistical significance, with multiple imputation method to handle missing data, as specified in the protocol for the trial. Additional preplanned statistical analyses of the primary endpoint data, including complete cases ANCOVA, last observation carried forward ANCOVA, generalized estimating equations and mixed model repeated measures, demonstrated that, in each case, azeliragon produces statistically significant differences from placebo on ADAS-COG_{11} ($p<0.05$).

The results for global, functional, cognitive and behavioral secondary endpoints after 18 months were also favorable despite the study not being powered to show significance. In each of the CDR-SB, ADCS-ADL, MMSE and NPI, patients in the 5 mg/day dose arm of azeliragon demonstrated numerical improvement compared to the placebo arm. In particular, the CDR-SB score improved by 0.7, the ADCS-ADL score improved by 1.4, the MMSE score improved by 1.0 and the NPI score improved by 1.2. In addition, the 5 mg/day treatment arm of azeliragon exhibited a statistically significant decrease in the incidence of psychiatric adverse events, including a statistically significant decrease in anxiety symptoms.

The results of the secondary endpoints in the ITT population are summarized in the following figures, which, in each case, illustrate a potential benefit of azeliragon versus placebo.

Azeliragon Effects on Global,

Functional, Behavioral and Cognitive Secondary Endpoints

ITT, Mild-to-Moderate AD (MMSE 14-26)

Prior to the completion of the analyses described above, a pre-specified interim safety analysis was conducted when 50% of subjects had completed the six-month visit. The 5 mg/day and placebo groups had no safety concerns. The high dose group was found to be associated with an increased incidence of confusion, falls and greater ADAS-COG_{11} decline than placebo and was discontinued. The 5 mg/day and placebo groups were allowed to continue without modification after all subjects were re-consented. The cognitive impairment and side effects in the high dose group were demonstrated to be reversible after discontinuing the study drug.

A second pre-specified interim analysis was conducted approximately 12 months after all subjects were randomized to compare the 5 mg/day dose versus placebo for futility and safety. While this second pre-specified interim analysis also raised no concerns regarding safety in the low-dose group, the criterion for futility was met, and the Data Safety Monitoring Board ("DSMB"), recommended discontinuation of the study. Pfizer elected then to discontinue the study. The futility analysis was conducted using data from only 84 patients, rather than the full population of 266 patients, and the data used in the analysis had not yet undergone rigorous database monitoring and error correction. Prior to the final database lock but after the decision to discontinue the study, data entry and scoring errors were found and corrected. Subsequent to the final database lock, we and independent statisticians attempted to replicate the results of Pfizer's futility analysis but were unable to do so.

In accordance with the protocol-specified statistical analysis plan, Pfizer and the ADCS performed the analysis of the 5 mg/day dose with respect to the primary ADAS-COG_{11} endpoint and the secondary endpoints, which produced the positive results described above. Additional analyses that we conducted subsequently also produced results consistent with the results of the protocol-specified analysis. Pfizer reverted the program to us in September 2011 and retains no residual economic rights in the program.

Efficacy in Mild AD Patients

Azeliragon at the 5 mg/day dose showed more pronounced efficacy in the mild AD sub-population (MMSE score 21-26) compared to patients with moderate AD (MMSE score 14-20). In the mild AD sub-population, azeliragon exhibited a statistically significant 4.0-point difference (p=0.018) in the ADAS-COG_{11} score relative to the placebo arm. In addition, while the study was not powered to show statistical significance in global, functional, behavioral and cognitive secondary endpoints, the mild AD sub-population demonstrated more pronounced favorable effects in those endpoints, including a statistically significant 1.0-point difference in the CDR-SB score (p=0.02) compared to the placebo group. The additional secondary endpoints demonstrated numerical improvements of 3.2 for the ADCS-ADL score, 1.1 for the MMSE score and 3.1 for the NPI score.

The results of the primary ADAS-COG_{11} endpoint in the mild AD population are summarized in the figure below.

The results of the secondary endpoints in the mild AD population are summarized in the following figures, which, in each case, illustrate potential benefits of azeliragon versus placebo.

Azeliragon Effects on Global,
Functional, Behavioral and Cognitive Secondary Endpoints
Mild AD (MMSE 21-26)

Adverse Events

Among the most frequent adverse events (“AEs”) in patients who received the high dose (20 mg/day) of azeliragon were falls (30 / 22.2%), urinary tract infection (“UTI”) (24 / 17.8%), diarrhea (20 / 14.8%), fatigue (19 / 14.1%), dizziness (12 / 8.9%), confusional state (10 / 7.4%) and headache (9 / 6.7%). Falls and UTI were also among the most frequent AEs in patients who received the low dose (5 mg/day) of azeliragon and placebo. The incidences of falls and UTI in the low-dose treatment group were 26 (19.8%) and 21 (16.0%), respectively; the incidences of falls and UTI among patients who received placebo were 26 (19.7%) and 17 (12.9%), respectively.

Of particular note, there was a statistically significant lower incidence of psychiatric AEs in patients receiving 5 mg/day compared to placebo. This was evidenced by a statically significant lower incidence of anxiety symptoms with numerically lower incidence of agitation, depression, sleep disorders, restlessness, aggression and confusion/disorientation.

No marked mean vital signs results or changes from baseline were observed in the active treatment groups compared to subjects who received placebo. There were no significant differences in laboratory blood or urine parameters or ECG changes between the three groups. No MRI findings of amyloid-associated imaging abnormalities (“ARIA”) were seen.

The high dose (20 mg/day) azeliragon arm was discontinued due to an increased incidence of confusion, falls, and an apparent accelerated cognitive decline suggested by a greater change over time in ADAS-COG_{11} score at a pre-specified interim analysis by an independent DSMB. There were no safety concerns evident in the 5 mg/day dose or placebo and these groups were permitted to continue the trial following re-consenting of subjects. The cognitive impairment and side effects in the 20 mg/day dose were demonstrated to be reversible after discontinuing the study drug. The trajectory of the ADAS-COG_{11} change from baseline curve over time not only showed the reversal of the transient cognitive worsening but ultimately crossed the placebo curve suggesting a possible underlying effect on the disease process. The mechanism behind the central nervous system (“CNS”) toxicity is unclear, but there were no signs of increased brain atrophy, no change in CSF and plasma levels of A , and no detected amyloid-related imaging abnormalities in the high-dose group.

Our Diabetes Programs – Glucokinase Activator and GLP-1r Agonist

Overview

Our lead diabetes drug candidates consist of our GKA (TTP399), for which we have completed patient enrollment in the Phase 2b AGATA Study, and our GLP-1r agonist (TTP273), for which we have completed Phase 1 trials and commenced a Phase 2 trial in early 2016. In previous studies, both TTP399 and TTP273 have been safe and tolerable and have demonstrated early signs of efficacy in both healthy volunteers and diabetes patient populations. We believe that these results show that our diabetes programs have the potential to provide superior efficacy and safety profiles versus existing compounds. We believe that TTP399 will be a first-in-class

OAD due to its liver selectivity and novel mechanism of action. We believe that TTP273 is positioned as a best-in-class GLP-1r agonist, providing type 2 diabetes patients with the only orally administered, small molecule, non-peptide GLP-1r agonist.

Diabetes Market Opportunity

A person suffering from type 2 diabetes does not produce or properly use insulin (a hormone necessary for allowing uptake of sugar from the bloodstream so that it may be converted into energy). In type 2 diabetes, the secretion of insulin from the pancreas and the action of insulin on tissues such as fat and muscle are both abnormal. Type 2 diabetics produce insulin, but insulin production and use both decrease over time as the disease progresses, ultimately requiring insulin administration to manage the disease. Obesity is generally considered the major contributor to the development of type 2 diabetes. As the global obesity epidemic expands, the increase in the number of type 2 diabetes patients is expected to continue. With the increasing incidence and prevalence of type 2 diabetes, we believe there is a significant unmet medical need for treatment alternatives with improved efficacy and safety.

Current Treatments for Diabetes and Their Limitations

The current treatment paradigm for diabetes focuses on lifestyle changes, including weight loss, if applicable, as well as medications to manage blood glucose levels. Obesity is generally considered the major contributor to the development of type 2 diabetes, and weight loss alone is associated with improvements in glycemic parameters. Optimal glycemic control is the treatment goal in diabetic patients to prevent the risk of long-term microvascular complications. There are currently several classes of drugs approved to improve glycemic control in patients with diabetes, including injectable drugs and OADs. Existing injectable therapies include most forms of insulin therapy and GLP-1r agonists. Existing OADs include metformin, sulfonylureas and thiazolidinediones, with the addition of two new classes in the past few years, DPP-4 and SGLT-2 inhibitors, driving the OAD market's growth. Despite the range of available therapies, diabetic patients have difficulty achieving and maintaining consistent glycemic control, defined as $HbA_{1c} < 7\%$ as recommended by the American Diabetes Association, and eventually progress to insulin use. Failure to attain or maintain glycemic control over time raises a patient's risk of disease progression with the attendant loss of control and progression to potentially serious complications, such as cardiovascular disease, blindness, kidney failure, and nerve damage. We believe the continued and significant unmet medical need for diabetes treatments is demonstrated by the commercial success of DPP-4 inhibitors, a new class of OADs which were first approved in the United States in 2006 and achieved annual sales of $5.2 billion in 2013.

We expect our diabetes drug candidates to compete in the non-insulin therapy market, currently comprised of OADs and injectable GLP-1r agonists. OADs are the preferred first line treatment by physicians (primary care and endocrinologists), payors and patients given their ease of use, convenience and no training requirements. The goal of these therapies is to delay the progression to insulin dependence (see the figure below). Despite the availability of multiple oral therapies and the introduction of new oral therapies (DPP-4 and SGLT-2 inhibitors) with novel mechanisms, used both as monotherapy and in combination with other agents, there remains a lack of differentiation and inadequate efficacy. While GLP-1r agonists are generally considered to have superior efficacy compared with OADs, primary care physicians and patients continue to prefer oral agents for their ease of use and improved patient compliance versus injectables. There remains an unmet medical need in the OAD class for a drug that mimics the superiority of GLP-1r agonists and reduces the incidence of hypoglycemia.

Progression of type 2 diabetes and treatment intensification using commonly prescribed oral and injectable diabetes drugs is summarized below.

With the increasing incidence and prevalence of type 2 diabetes, we believe there is a significant unmet medical need for treatment alternatives with improved efficacy and safety. We have chosen two different approaches for the treatment of diabetes: activation of GK, through our drug candidate TTP399, and stimulation of GLP-1r, through our drug candidate TTP273. If approved, we believe TTP399 and TTP273 could offer attractive alternatives as OADs for the treatment of type 2 diabetes.

Glucokinase Activator

The Role of GK Activation in Diabetes

GK acts as the physiological glucose sensor, changing its conformation, activity and/or intracellular location in parallel with changes in glucose concentrations. GK has two main distinctive characteristics that make it a good choice for blood glucose control. First, its expression is mostly limited to tissues that require glucose-sensing (mainly liver and pancreatic -cells). Second, GK is able to sense changes in serum glucose levels and modulate changes in liver glucose metabolism that in turn regulate the balance between hepatic glucose production and glucose consumption, and modulate changes in insulin secretion by the -cells.

Studies in humans, along with numerous animal studies, showing that mutations in the gene encoding GK can cause both hyperglycemia (diabetes mellitus) and hypoglycemia (glucose levels below normal) depending on the mutation, confirm the critical role of GK in the regulation of glucose control. The concept of GK activation for the treatment of diabetes is attractive because it has proven to be effective and safe in normalizing glycemia in animal models of type 2 diabetes by a mechanism entirely distinct from the action of antidiabetic therapies currently on the market. Moreover, several lines of evidence have suggested that development of type 2 diabetes is related to functional impairment of the GK enzyme. Thus, GK activation may be a way to overcome an important underlying cause of type 2 diabetes progression and hence halt or delay the course of the disease.

Our approach to targeting GK is to use a small molecule, liver-selective compound that only activates GK in the liver without affecting the interaction between GK and glucokinase regulatory protein (“GKRP”). Many competitors have tried to develop drugs that act as GKAs. Previously identified GKAs evaluated in the clinic for the treatment of type 2 diabetes demonstrate improved

glucose control; however, these GKAs showed increased incidence of hypoglycemia and hyperlipidemia and an apparent lack of durability. These liabilities have been correlated to hyperstimulation of the -cells in a glucose independent manner and/or the accumulation of lipids in the liver, consistent with the disruption of GK and the GKRP interaction by these GKAs. Thus, liver-selective compounds that do not activate GK in pancreatic -cells or affect the GK-GKRP interaction in the liver are expected to demonstrate a superior profile in comparison to previously identified GKAs.

Our Solution: Glucokinase Activator

TTP399 is an orally administered, small molecule, liver-selective GKA in development as a new OAD for the treatment of type 2 diabetes with a novel mechanism of action. Activation of GK provides intensive glycemic control without inducing hypoglycemia. If approved, we believe TTP399 would compete primarily with OADs, including DPP-4 and SGLT-2 inhibitors. Our trials for TTP399 suggest that our approach to GK activation has the potential to avoid safety and tolerability issues associated with other GKAs, such as activation of GK in the pancreas, stimulation of insulin secretion independent of glucose, hypoglycemia, increased lipids and liver toxicity. Further, we believe that TTP399, if approved, has the potential to be more effective than competing non-insulin products, the potential to normalize HbA_{1c} levels, the potential for no contraindication for renal impairment and no risk of pancreatitis. We believe that TTP399 has the potential to be a first-in-class OAD due to its liver-selectivity and novel mechanism of action.

Glucokinase Activator Clinical and Regulatory Overview

We have completed patient enrollment in the AGATA Study, a 180-patient Phase 2b clinical study for TTP399. We initiated the AGATA Study based upon the results of TTP399-201, a Phase 2a clinical trial that demonstrated TTP399 has the ability to improve glycemic control after six weeks of treatment. We have completed ten clinical trials of TTP399, summarized in the table below. In our Phase 1 and 2 clinical trials, TTP399 was safe and well tolerated without any episodes of hypoglycemia.

Study	Phase	Objectives	Completion Date
AGATA	Phase 2b	Multiple site, six-month, double-blind, parallel, repeat-dosing study to evaluate safety and efficacy	Est. mid-2016
TPP399-201	Phase 2a	Multiple site, six-week double-blind, parallel, repeat-dosing study to characterize PK and PD profiles in type 2 diabetes patients not well controlled on metformin	September 2012
GK01-117	Phase 1	A drug-drug interaction study with statins	October 2012
GK01-115	Phase 1	An open-label, single-dose, four-way crossover study in 30 healthy male subjects to compare PK of four formulations	November 2011
GK01-115	Phase 1	Single dose study healthy volunteers (“HV”) absolute and regional bioavailability	August 2011
TTP399-107	Phase 1	Capsule versus tablet bioavailability	May 2010
TTP399-106	Phase 1b	Ten day multi-dose study in diabetic patients not controlled on metformin	November 2010
TTP399-104	Phase 1	Single dose study HV encapsulated tablet	April 2009
TTP399-103	Phase 1	Ten day multi-dose study in HV	June 2009
TTP399-102		Ten day multi-dose study in naïve diabetics	August 2008

	Phase 1b		
TTP399-101	Phase 1	Single dose study in HV	December 2007

Ongoing Phase 2b AGATA Study

In March 2015, we initiated a Phase 2b clinical trial of TTP399, the AGATA Study, which is a six-month trial to demonstrate proof-of-concept that the benefits from TTP399 can be sustained over time. The AGATA Study is a multi-center adaptive Phase 2b, randomized, double-blind, placebo- and active- (sitagliptin) controlled, parallel group trial to evaluate the safety and efficacy of TTP399 following six months of administration in 180 subjects with type 2 diabetes on a stable dose of metformin. Patients will have a baseline HbA_{1c} of 7.0-9.5%. The AGATA Study include subjects across four arms, including two doses of TTP399 (400 mg and 800 mg), sitagliptin, which is a DPP-4 inhibitor, and placebo.

The primary endpoint of the AGATA Study will be the change from baseline in HbA_{1c} at six months. The secondary endpoints will include subject achievement of $HbA_{1c} < 7\%$ at six months, subject achievement of $HbA_{1c} < 6.5\%$ at six months, plasma glucose, lipids (triglycerides, total cholesterol, HDL cholesterol, and LDL cholesterol), insulin, lactate, C-peptide, glucagon, GLP-1 and body weight. The study has completed and we expect topline data from the AGATA Study in mid-2016.

Completed Phase 2a Clinical Trial (TTP399-201)

We completed a six-week Phase 2a clinical trial of TTP399, a randomized, double-blind, parallel-group, placebo-controlled, multiple dose study in 120 type 2 diabetes patients whose glycemic parameters were not well-controlled on metformin. The trial was

designed to assess the pharmacokinetics, pharmacodynamics, safety and tolerability of TTP399 and was conducted at 11 centers in the United States. Patients were randomized into four arms: 29 received TTP399 400 mg twice a day ("BID"), 31 received TTP399 800 mg once a day ("QD"), 30 received TTP399 800 mg BID and 30 received placebo. All patients remained on consistent doses of metformin throughout the trial. HbA_{1c} was generally consistent across arms in the trial with an average of approximately 8.2%.

In the trial, TTP399 demonstrated a statistically significant reduction in HbA_{1c} levels in all TTP399 dose groups compared with placebo, without induction of hypoglycemia or hyperlipidemia and with no induction of insulin secretion in patients with type 2 diabetes. Moreover, TTP399 normalized glycemia, defined as $HbA_{1c} \leq 6.5\%$, after only six weeks of treatment. Specifically, within the high dose arm of TTP399, approximately 86% of patients with HbA_{1c} levels $\leq 7.5\%$ at baseline achieved blood glucose normalization, defined as $HbA_{1c} \leq 6.5\%$, after six weeks of treatment, while 50% of patients with HbA_{1c} levels $\leq 8\%$ at baseline achieved normalization after six weeks. For all doses combined, approximately 40% of patients with HbA_{1c} levels $\leq 7.5\%$ at baseline achieved blood glucose normalization while 25% of patients with HbA_{1c} levels $\leq 8\%$ at baseline achieved normalization. None of the patients receiving placebo reached HbA_{1c} normalization.

The results showing the reduction in HbA_{1c} in all subjects and the subgroup with HbA_{1c} levels $\leq 7.5\%$ at baseline are summarized in the following figures:

Clinical results also showed a statistically significant effect on both postprandial glucose, fasting glucose, average daily glucose and no increases on fasting plasma lipids or plasma lactate.

Adverse Events

TTP399 was generally safe and well tolerated at all doses in the trial. The proportion of patients reporting at least one AE was between 42% to 63% in the TTP399 groups compared to 40% in the placebo group. There was no notable imbalance in the reporting of any AE between the active trial and the placebo. There were no AEs that led to discontinuation of study drug. There was no dose-responsive increase in the percentages of subjects with at least one AE. One subject in the 800 mg QD group experienced a moderate severe AE of diverticulitis on Day 15 that was considered not related to study drug. No action was taken with study drug, and the event resolved ten days later.

GLP-1r Agonist

The Role of GLP-1r Activation in Diabetes

GLP-1r is a class B, G protein-coupled receptor that regulates important physiological and pathological processes related to type 2 diabetes. GLP-1r stimulation as a therapeutic modality has been validated by the approval of peptide GLP-1r agonists, such as exendin-4 (Byetta) and liraglutide (Victoza). Subcutaneous administration of these peptides lowers blood glucose, decreases HbA_{1c} levels and reduces weight. This class of peptides is associated with gastrointestinal side effects (nausea and vomiting). Despite the clinical success observed with the injectable peptides, no orally available GLP-1r agonists have demonstrated similar success to date.

Our Solution: GLP-1r Agonist

GLP-1r agonists, including exenatide (Byetta, Bydueron), albiglutide (tanzeum) and liraglutide (Victoza), are well established in terms of efficacy, but their use has been limited due to their administration as an injectable. Subcutaneous administration of these peptides lowers blood glucose, decreases HbA_{1c} levels and reduces weight. However, this class of peptides is associated with gastrointestinal side effects including nausea and vomiting. TTP273 is a potential first-in-class, orally administered, small molecule, non-peptide GLP-1r agonist. Our past proof-of-concept study with our first generation product, TTP054, demonstrated efficacy consistent with marketed GLP-1r agonists, and our trials indicated that TTP273 may have superior tolerability compared to competing products, as shown through low incidence of gastrointestinal AEs and no antibody formation. We believe an orally administered GLP-1r agonist that mimics the metabolic effects of GLP-1r showing enhanced glycemic control, an improved lipid profile and weight loss, without causing the gastrointestinal side effects typical of this class of compounds, would offer a competitive advantage compared to GLP-1r targeted treatment options currently available. For these reasons, we believe TTP273 has the potential to expand the use of GLP-1r agonists for the treatment of type 2 diabetes.

GLP-1r Agonist Clinical and Regulatory Overview

We have completed two Phase 1 clinical trials of TTP273 providing for proof-of-principle achieved in humans. Additionally, we have completed ten Phase 1 and Phase 2 clinical trials of TTP054, which was a predecessor orally administered GLP-1r agonist. In our Phase 1 and Phase 2 clinical trials, TTP273 and TTP054 have been safe and well tolerated. Based on the results of our completed Phase 1 and 2 clinical trials of TTP273 and TTP054, we believe our orally administered GLP-1r agonists have the potential to provide both superior efficacy and tolerability versus peptide GLP-1r analogues. We have commenced a Phase 2 clinical trial of TTP273 to show proof-of-concept that TTP273 can significantly reduce HbA_{1c} and body weight over a twelve week period. The trial is expected to include approximately 156 subjects in three different groups, including two arms that will receive TTP273 and a placebo arm. We expect to report topline data on this trial in late 2016. These trials are summarized in the table below.

Study	Phase	Objectives	Completion Date
TTP273			
LOGRA	Phase 2	Multiple site, randomized, double blind, placebo-controlled, parallel group trial in type 2 diabetics on stable doses of metformin	Est. late 2016
TTP273-102	Phase 1b	14-day multiple dose (“MD”) study in diabetic patients not controlled on metformin	November 2013
TTP273-101	Phase 1	Single dose (“SD”) study in healthy volunteers	October 2012
TTP054			
TTP054-201	Phase 2	12-week MD in patients with type 2 diabetes on stable doses of metformin	June 2013
TTP054-111	Phase 1	SD, crossover, in HV to compare table formulations	August 2012
TTP054-110	Phase 1	SD in patients with type 2 diabetes	March 2012
TTP054-109	Phase 1	SD in HV to compare table formulations	October 2011
TTP054-108	Phase 1b	28-day MD in patients with type 2 diabetes on stables doses of metformin	November 2011
TTP054-106	Phase 1	SD in HV (tablet formulation)	December 2010
TTP054-104	Phase 1b	14-day MD in patients with type 2 diabetes (liquid formulation)	August 2010
TTP054-103	Phase 1	SD, crossover, modified-glucose-infusion in HV to study insulin secretion	March 2009
TTP054-102	Phase 1b	10-day multi-dose study in naïve diabetics	July 2010

TTP054-101 Phase 1	Single dose study in healthy volunteers	July 2008

Completed Phase 2 Clinical Trial

Our completed Phase 2 clinical trial of TTP054 was a randomized, double-blind, parallel-group, placebo-controlled, 12-week, multiple dose study in 187 randomized type 2 diabetic patients who were not well-controlled on metformin. The trial was designed to assess the safety and efficacy of TTP054. The trial was conducted at 19 centers in the United States. Patients were randomized into four arms: 28 to receive TTP054 200 mg/day, 51 to receive TTP054 400 mg/day, 56 to receive TTP054 800 mg/day and 52 to receive placebo. The primary efficacy endpoint of the trial was change from baseline in HbA_{1c} as compared to placebo. The secondary endpoints included change from baseline in fasting plasma glucose, subject achievement of HbA_{1c} <7%, change from baseline in body weight, and subject achievement of body weight loss ≥ 2%.

Our proof-of-concept trial showed statistically significant placebo-corrected reductions in the average level of blood sugar as measured by HbA_{1c}. In the trial, there was a reduction of 1% HbA_{1c} in subjects not well-controlled on metformin after 12 weeks of treatment. The efficacy demonstrated was consistent with published data for marketed GLP-1 mimetics (exenatide) in studies of similar duration.

Adverse Events

These clinical trials showed that our GLP-1r agonists have negligible incidences of AEs and no increased risk of hypoglycemia when compared to placebo. In our completed Phase 2 trial, a total of 178 AEs were reported by 69 of 184 patients, or 38%. The proportion of patients reporting at least one AE was highest in the TTP054 800 mg/day dose group at 45% versus 40% in the placebo group. The proportion of patients that reported at least one AE were lowest in the 400 mg and 200 mg dose groups at 27% and 37%, respectively.

Overall, in our Phase 2 trial, TTP054 was safe and well-tolerated. There were no hypoglycemia AEs, and GI AEs, including nausea and vomiting, were minimal and similar in incidence and severity in active and placebo groups. There were five subjects with AEs that were considered serious and led to discontinuation from the study. Among these subjects, only two AEs occurred in TTP054-treated subjects (increases in LFTs without increased bilirubin) and were considered related to TTP054. All of these AEs resolved with no sequelae.

TTP273 was generally safe and well-tolerated in our completed Phase 1 clinical trials, with no severe AEs reported after up to 14 days of dosing. There was no apparent dose relationship and no hypoglycemic incidents.

Additional Pipeline Opportunities

Oncology – Hexokinase II Inhibitors

The field of tumor metabolism seeks to exploit the unique ways in which cancer cells take up and utilize nutrients in order to grow and proliferate. Cancer cells have altered cellular metabolic pathways to acquire and utilize these nutrients and redirect them to provide the necessary building blocks for growth. When these metabolic pathways are blocked, cancer cells are essentially starved of critical nutrients and stop growing or die, whereas normal cells are largely unaffected.

Most cancer cells have increased uptake of the sugar glucose relative to surrounding normal cells. This phenomenon forms the basis for the widely used tumor imaging procedure known as 18F-2-deoxyglucose (FDG)/PET. Tumors take up more FDG, a radioactive glucose analog, than the surrounding normal tissue and this differential can be visualized with PET imaging. Not only do tumors take up more glucose, they also utilize the nutrient in a unique way. Tumors convert glucose into lactic acid in a process known as aerobic glycolysis or the “Warburg effect,” a route rarely utilized in normal cells. This unique uptake and processing of glucose by tumors relative to normal tissue creates an opportunity to selectively target tumors by cutting off their ability to use this fuel.

In many cancers, hexokinase II is overexpressed and has been linked to more aggressive and invasive tumors. Pre-clinical studies in mice have confirmed that the reduction of hexokinase II activity through genetic deactivation (siRNA knockdown studies)

results in a significant reduction of tumor growth. Our hexokinase inhibitors may provide an opportunity to inhibit the unique way cancer cells utilize glucose, and the overall Warburg effect, which could result in new treatments for cancer.

Calithera Biosciences, Inc. ("Calithera") has exclusive, worldwide rights to our hexokinase II inhibitors for research, development and commercialization. We have received an initial license fee from Calithera, and Calithera will pay us potential development and regulatory milestone payments and royalty payments under the agreement.

Other Candidates

We are also developing a portfolio of additional clinical drug candidates for the prevention of muscle weakness associated with PMV and critical injury, as well as the treatment of inflammatory disorders. These additional candidates have been through varying stages of preclinical and Phase 1 testing and we have submitted investigational new drug applications ("INDs") for certain of them to the FDA. While our primary focus is on the clinical trials involving azeliragon, TTP399 and TTP273, we plan to continue to evaluate opportunities for furthering the development of these other compounds in our pipeline. Such development many be done internally or through partnering relationships.

Our Proprietary Technology Platform

We use a proprietary drug discovery platform that facilitates the discovery of novel drug candidates in a time- and cost-efficient manner. Using this discovery technology, we have completed the discovery phase for some of its most promising candidate drugs in weeks and months, as compared to an industry average of two to three years, and with this technology, we expect to similarly be able to reduce the discovery phase for any future drug candidates.

TTP Translational Technology

We developed a proprietary drug discovery platform called TTP Translational Technology, which we use to discover novel small molecule therapeutics for major diseases and to validate biological pathways and targets. All of the small molecule drug candidates in our pipeline (other than HPP593) were discovered using TTP Translational Technology.

TTP Translational Technology is a fully integrated drug discovery process, amenable to automation, which works to translate genomic and proteomic data into safe and effective small molecule therapeutics in high-throughput fashion, bypassing most of the classical requirements and bottlenecks in drug discovery. We have used this technology to discover drugs for our internal pipeline and in research collaborations with pharmaceutical and biotechnology companies.

Our Integrated Platform

TTP Translational Technology consists of three modules that are fully integrated with an informatics system that captures data from each optimization cycle of the drug discovery process. This informatics system is built with a sophisticated architecture that supports various computing platforms and provides automatic archiving and storage capabilities. The three modules comprising TTP Translational Technology are:

· TTPredict provides modeling tools, simulations, statistical and analysis algorithms and visualization in one package. The resulting molecular discovery process couples high throughput in silico and in biologico screening data with extensive automation in a parallel and integrated fashion in order to rapidly develop hypotheses concerning novel protein structures and potential ligand binding sites. The system uses high-throughput virtual docking, ranking and screening and employs multiple scoring methods. These operations are encompassed within component modules known as TTPostGene, TTPSite, TTPDock and TTPSelect.

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TTPSpace is a proprietary library of diverse, drug-like, well characterized compounds (TTProbes and related compound libraries) that can be used in our automated drug discovery processes. We have the capacity to synthesize hundreds if not thousands of well-characterized compounds per day in milligram quantities. TTProbes are an ensemble of functionally diverse, structurally unique and nested low molecular weight molecules exemplifying key recognition elements that enable an immediate interpretation and subsequent extrapolation of the geometric, stereo-electronic and physiochemical requirements for binding to target proteins. These molecular probes deliver a focused yet adjustable technique for lead discovery or target validation, especially when coupled to the computational capabilities embodied in TTPredict. TTProbes are tools for rapid biological target validation, bypassing the often time-consuming process of classical pharmacology requirements, quickly producing data about essential binding elements between biological targets and small molecule modulators. Selectivity and specificity data is generated much earlier compared to hits against a classical library, while minimizing negative prior art issues.

- TTPScreen consists of novel translational biology techniques, including genomic and high-content imaging processes and proprietary tools built with a sophisticated architecture that supports various computing platforms and utilizes dynamic scripting

and parallel execution, allowing management of large amounts of biological data generated from high-throughput screening, including complex experimental protocols, flexible and dynamic assay layouts, multiple IC50 determinations, interactive profiling and kinetic studies. TTPScreen allows full utilization and access to all the available biological and chemical data and information in a highly integrated fashion.
TTP Translational Technology reduces manual tasks, provides rapid validation, lead discovery and optimization of novel clinical candidates, reduces prior art issues associated with leads pulled from classical sources and is capable of addressing the need and demand for complex, non-traditional biological targets such as protein-protein interactions.

Our average time from biological concept through completion of Phase 1 trials is about four to five years, which is half of the industry average, helping to lower costs and enhance the speed of drug development. Our development methods can be used to identify targets in various therapeutic areas and are scalable to support a large number of programs.

Third-Party Suppliers and Manufacturers

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties to manufacture clinical supplies of our drug candidates and for our other research and discovery programs.

Intellectual Property

Patents

The IP portfolio for azeliragon includes a patent family covering azeliragon as a composition of matter, a patent family covering polymorphs of azeliragon and a patent family covering select methods of treatment using azeliragon. Azeliragon as a composition of matter is covered by issued patents in the United States, Europe, Japan, Canada, Australia, China and Hong Kong. The issued U.S. patent covering azeliragon as a composition of matter is expected to expire in 2029, assuming we obtain the maximum possible extension. Patents covering azeliragon as a composition of matter outside the United States will expire no earlier than 2023 and may expire much later as a result of patent term extensions based on patent office delays, regulatory delays, or a combination thereof.

The IP portfolio for TTP399 includes a patent family covering TTP399 as a composition of matter, a patent family covering combinations of TTP399 and metformin, a patent family covering combinations of TTP399 and DPP-4 inhibitors or GLP-1r agonists, and patent families covering two different solid formulations of TTP399. The patent family covering TTP399 as a composition of matter was filed in multiple jurisdictions around the world including the United States, Europe, Japan and Canada. The issued U.S. patent covering TTP399 as a composition of matter is expected to expire in 2030, assuming we obtain the maximum possible extension. Patents covering TTP399 as a composition of matter outside the United States will expire no earlier than 2025 and may expire much later as a result of patent term extensions based on patent office delays, regulatory delays, or a combination thereof. Some patents and patent applications covering TTP399 as a composition of matter are licensed from Novo Nordisk A/S, while others are owned by us.

The IP portfolio for the GLP-1r program includes a patent family covering TTP054 as a composition of matter, a patent family covering TTP273 as a composition of matter, a patent family covering specific salts of TTP054, a patent family covering combinations of TTP054, or TTP273, and metformin, and a patent family covering methods of synthesizing precursors to TTP054 and TTP273. The patent family covering TTP054 as a composition of matter was filed in multiple jurisdictions around the world including the United States, Europe, Japan and Canada. The issued U.S. patent covering TTP054 as a composition of matter is expected to expire in 2034, assuming we obtain the maximum possible extension. Patents covering TTP054 as a composition of matter outside the United States will expire no earlier than 2029 and may expire much latter as a result of patent term extensions based on patent office delays, regulatory delays, or a combination thereof. The patent family covering TTP273 as a composition of matter

was filed in multiple jurisdictions around the world including the United States, Europe, Japan and Canada. The issued U.S. patent covering TTP273 as a composition of matter is expected to expire in 2034, assuming we obtain the maximum possible extension. Patents covering TTP273 as a composition of matter outside the United States will expire no earlier than 2030 and may expire much later as a result of patent term extensions based on patent office delays, regulatory delays or a combination thereof.

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. For example, significant aspects of our TTP Translational Technology are based on unpatented trade secrets and know-how. Trade secrets and know-how can be difficult to protect, and a number of the individual components of our TTP Translational Technology are now commercially available. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality

agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed by employees or through a relationship with a third party. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become publicly known or be independently discovered by competitors. To the extent that our contractors use or incorporate intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

License Agreements

Calithera

In March 2015, we entered into a License and Research Agreement with Calithera (the "Calithera License Agreement"), under which Calithera obtained an exclusive, worldwide, sublicensable license to develop and commercialize certain of our hexokinase II inhibitors for any therapeutics, prophylactic, preventative or diagnostic use.

Under the terms of the Calithera License Agreement, Calithera paid us an initial license fee of $600,000, and will pay us potential development and regulatory milestone payments totaling up to $30.5 million for the first licensed product. We are eligible for an additional $77.0 million in potential sales-based milestones, as well as royalty payments, at mid-single digit royalty rates, based on tiered sales of the first commercialized licensed product. In addition, Calithera will fund up to $1.1 million during the first 12 months of the Calithera License Agreement for the costs associated with up to four of our full-time employee equivalents to develop additional hexokinase inhibitors. If Calithera develops additional licensed products, after achieving regulatory approval of the first licensed product, Calithera would owe additional regulatory milestone payments and additional royalty payments based on sales of such additional licensed products.

Except for the research program funded by Calithera with us, Calithera will be responsible for the worldwide development and commercialization of the licensed products, at its cost, is required to use commercially reasonable efforts with respect to such development and commercialization activities, and must meet certain specified diligence obligations. Calithera holds the first right to prosecute and to enforce all licensed patents under the Calithera License Agreement throughout the world, and we will retain certain step-in prosecution and enforcement rights.

The Calithera License Agreement, unless terminated earlier, will continue on a product-by-product and country-by-country basis until expiration of the royalty obligations Calithera owes to us on such licensed product, which extend until the later of the expiration of certain patent or data exclusivity rights covering such licensed product in such country or ten years after the first commercial sale of such product in such country. Either party may terminate the Calithera License Agreement for the other party's uncured material breach. Calithera may terminate the Calithera License Agreement at will upon prior written notice. Either party may terminate the Calithera License Agreement for the other party's insolvency.

Novo Nordisk

In February 2007, we entered into an Agreement Concerning Glucokinase Activator Project with Novo Nordisk A/S (the "Novo License Agreement") whereby we obtained an exclusive, worldwide, sublicensable license under certain Novo Nordisk intellectual property rights to discover, develop, manufacture, have manufactured, use and commercialize products for the prevention, treatment, control, mitigation or palliation of human or animal diseases or conditions. As part of this license grant, we obtained certain worldwide rights to Novo Nordisk's GKA program, including rights to preclinical and clinical compounds such as TTP399. Under the terms of the Novo License

Agreement, we have additional potential developmental and regulatory milestone payments totaling up to $115.0 million for approval of a product. We are also obligated for an additional $75.0 million in potential sales-based milestones, as well as royalty payments, at mid-single digit royalty rates, based on tiered sales of commercialized licensed products.

Columbia University

In May 2015, we entered into a New Exclusive License Agreement (the “Columbia License Agreement”) with The Trustees of Columbia University in the City of New York (“Columbia”) whereby by we obtained a worldwide, exclusive license, with the right to grant sublicenses under certain Columbia RAGE-related patent rights to discover, develop, manufacture, use, sell, have sold, import, have made, offer to sell, rent, or lease RAGE-inhibiting small molecules, including azeliragon. We also obtained a worldwide right to use certain RAGE-related research information and material. Under the terms of the Columbia License Agreement, we are required to pay an annual fee of $0.1 million, a potential milestone payment of $0.8 million and royalty payments at low-single digit royalty rates

based on the net sales of licensed products. At the end of 2021, any fees and payments under the agreement will end, and we will have an irrevocable license to the RAGE-related patent rights, research information and material.

Competition

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical companies and generic drug companies. We believe the key competitive factors that will affect the development and commercial success of our drug candidates are efficacy, safety and tolerability profile, mechanism of action, control and predictability, convenience of dosing and price and reimbursement.

Many of the companies against which we may compete have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Potential Competing Products – Alzheimer's Disease

There are currently no approved disease-modifying treatments for AD in the United States, as existing therapies treat only the symptoms of the disease, rather than targeting the underlying mechanisms. The approved symptomatic AD therapies in the United States fall into two classes, AChEIs and glutamatergic modulators. If azeliragon is approved, its mechanism of action may be complementary to that of drug candidates with differentiated mechanisms currently in development as potential disease modifying treatments for AD, including anti-A monoclonal antibodies, BACE inhibitors, tau aggregation inhibitors and monoamine oxidase-b inhibitors. This will allow the opportunity for co-administration with these other drug candidates if they are successfully developed. We are not aware of any other clinical-stage RAGE inhibitors for the treatment of AD.

Potential Competing Products – Type 2 Diabetes

We expect that our type 2 diabetes drug candidates will compete with currently available non-insulin medication products for type 2 diabetes. These products include the following:

- Injectable GLP-1r agonists, such as exenatide or liraglutide, which mimic a naturally occurring hormone that stimulates the pancreas to secrete insulin when blood glucose levels are high.
- DPP-4 inhibitors, such as sitagliptin or saxagliptin, are a class of drugs that work by blocking the enzyme that normally degrades GLP-1.
- Sulfonylureas and meglitinides, which are classes of drugs that act on the pancreatic cells to stimulate the secretion of insulin.
- Thiazolidinediones, such as pioglitizone, and biguanides, such as metformin, which lower blood glucose by improving the sensitivity of cells to insulin, or diminishing insulin resistance.
- Alpha-glucosidase inhibitors, which lower the amount of glucose absorbed from the intestines, thereby reducing the rise in blood glucose that occurs after a meal.
- SGLT-2 inhibitors, such as dapagliflozin and canagliflozin, are a class of medications that lower blood glucose by increasing glucose excretion in urine.

In addition to existing marketed products, there are a number of product candidates currently in development focusing on the same mechanisms as our programs for the treatment of type 2 diabetes, including:

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- Glucokinase activators: Advinus Therapeutics Ltd., Eli Lilly and Company, Pfizer Inc., Hua Medicine Ltd. and Teijin Pharma Limited are among the companies evaluating glucokinase activators in clinical or preclinical studies.
- Oral GLP-1r agonists: Diabetology Ltd., Novo Nordisk, Oramed Pharmaceuticals Inc., Poxel SA and Receptos, Inc. are among the companies evaluating oral GLP-1r agonists in clinical or preclinical studies.

We believe that our drug candidates may offer key potential advantages over these competitive products that could enable our drug candidates, if approved, to capture meaningful market share from our competitors. Nevertheless, many of our potential competitors have substantially greater financial, technical and human resources than we do, as well as greater experience in the discovery and development of drug candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than us in obtaining regulatory approval for drugs and

achieving widespread market acceptance. Our competitors' drugs may be more effective, or more effectively marketed and sold, than any drug candidate we may commercialize and may render our drug candidates obsolete or non-competitive before we can recover the expenses of their development and commercialization. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. Finally, the development of new treatment methods for the diseases we are targeting could render our drug candidates non-competitive or obsolete.

Collaboration Revenue and Customers

The majority of our collaboration revenue and accounts receivable are related to the Calithera License Agreement described above. Currently, we do not believe the amounts of revenue generated under the Calithera License Agreement are material to us, since the compounds subject to the Calithera License Agreement are in the pre-clinical stage, and we are focused primarily on our Phase 3 clinical trial, the STEADFAST Study, with respect to azeliragon, and our Phase 2 clinical trials, with respect to TTP399 and TTP273.

Government Regulation and Product Approval

Government authorities in the United States at the federal, state and local level extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, export and import of products such as those we are developing. Our drug candidates must receive final approval from the FDA before they may legally be marketed in the United States.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, "FDCA", and implementing regulations. The process of obtaining regulatory approvals and ensuring compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process, or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a hold on clinical trials, warning letters, product seizures, product detention, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies according to Good Laboratory Practices or other regulations, as well as formulation studies;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCP, to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA for a new drug;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

The testing and approval process require substantial time, effort and financial resources, and we cannot be certain that any approvals for our drug candidates will be granted on a timely basis, if at all.

Once a pharmaceutical drug candidate is identified for development, it enters the preclinical testing stage. The preclinical testing stage includes laboratory evaluations of product chemistry, toxicity, formulation and stability, as

well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, to the FDA as part of the IND. The sponsor must also include a protocol detailing, among other things, the objectives of the initial clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the initial clinical trial lends itself to an efficacy evaluation. Preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during trials due to safety concerns or non-compliance.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations. These regulations include the requirement that all research subjects provide informed consent. Further, an institutional review board ("IRB"), must review and approve the plan for any clinical trial before it commences at any institution. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the information regarding the clinical trial and the consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Once an IND is in effect, each new clinical protocol and any amendments to the protocol must be submitted to the IND for FDA review, and to the IRBs for approval.

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

- Phase 1. The drug candidate is initially introduced into healthy human subjects and tested for tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing may be conducted in patients having the specific disease.
- Phase 2. Phase 2 trials involve investigations in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the drug candidate for specific targeted diseases and to determine optimal dosage and schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in a larger patient population, generally at geographically dispersed clinical trial sites. These trials are intended to establish the overall risk/benefit ratio of the drug candidate and provide an adequate basis for regulatory approval and product labeling.

Post-approval studies, also called Phase 4 trials, may be conducted after initial marketing approvals. These studies are used to obtain additional experience from the treatment of patients in the intended therapeutic indication and may be required by the FDA as part of the approval process.

Progress reports detailing the results of the clinical trials must be submitted annually to the FDA and safety reports must be submitted to the FDA and the investigators for serious and unexpected side effects. Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution on various grounds, including if the research subjects are being exposed to an unacceptable health risk.

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

Special Protocol Assessment

The special protocol assessment, or SPA, process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate the proposed design and size of Phase 3 clinical trials that are intended to form the primary basis for determining a drug product's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial design and data analysis plans, within 45 days of receipt of the request.

The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the drug candidate with respect to effectiveness of the indication studied. All agreements and

disagreements between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Even if the FDA agrees to the design, execution and analyses proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement under the following circumstances:

- public health concerns emerge that were unrecognized at the time of the protocol assessment, or the director of the review division determines that a substantial scientific issue essential to determining safety or efficacy has been identified after testing has begun;
- a sponsor fails to follow a protocol that was agreed upon with the FDA; or
- the relevant data, assumptions or information provided by the sponsor in a request for SPA change, are found to be false statements or misstatements, or are found to omit relevant facts.

A documented SPA may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study. We have obtained an SPA with the FDA for our Phase 3 STEADFAST Study of azeliragon. Agreement by the FDA to an SPA does not guarantee that the results of a study conducted in accordance with the agreement will be successful.

United States Review and Approval Processes

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the drug, proposed labeling and other relevant information, are submitted to the FDA as part of an NDA, requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees which may be waived under certain limited circumstances.

FDA Review of New Drug Applications

The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be re-submitted with the additional information. The re-submitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has ten months from the date the application is accepted for filing in which to complete the initial review of a standard NDA and respond to the applicant and six months for a priority NDA. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether the chemistry, manufacturing and control documentation is adequate to assure and preserve the product’s identity, strength, quality and purity. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA may refer the NDA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. An advisory committee is a panel of independent experts who provide advice and recommendations when requested by the FDA on matters of importance that come before the agency. The FDA is not bound by the recommendation of an advisory committee.

The approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information.

Even if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA in its present form. The complete response letter usually describes all of the specific deficiencies that the FDA identified in the NDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may

include recommended actions that the applicant might take to conform the application to a condition suitable for approval. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, withdraw the application, or request an opportunity for a hearing.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require Phase 4 testing which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA approval and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including Fast Track designation, accelerated approval and priority review, that are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a Fast Track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA may determine that a product will fill an unmet medical need if it is expected to provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors.

The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months from the date of filing of the NDA. Most products that are eligible for Fast Track designation are also likely to be considered appropriate to receive a priority review.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions and that provide meaningful therapeutic benefit over existing treatments may be eligible to receive accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Moreover, under the Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted in 2012, a sponsor can request designation of a drug candidate as a “breakthrough therapy.” A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We have obtained Fast Track designation for azeliragon for the treatment of dementia of the Alzheimer’s type.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA marketing approval of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining

term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally (a) one-half the time between the effective date of an IND and the submission date of an NDA plus (b) the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent and within 60 days of approval of the drug. The PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Data and market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent data and marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active pharmaceutical ingredient, or active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a Section 505(b)(2) NDA submitted by another company that references the previously approved drug with exclusivity. Section 505(b)(2) generally permits the submission of an NDA where at least some of the information required for approval comes from clinical trials not conducted by or for the applicant and for which the applicant has not obtained a right of

reference. However, an ANDA or Section 505(b)(2) application may be submitted after four years if it contains a Paragraph IV certification claiming that the patents covering the drug are either invalid or not infringed by the drug described in the ANDA or 505(b)(2) application.

The FDCA also provides three years of marketing exclusivity for an NDA, Section 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. Such clinical trials may, for example, support new indications, dosages, routes of administration or strengths of an existing drug, or a new use. This exclusivity, which is sometimes referred to as clinical investigation exclusivity, prevents the FDA from approving an ANDA or an application under Section 505(b)(2) for the same conditions of use associated with the new clinical investigations before the expiration of three years from the date of approval. Such three-year exclusivity, however, would not prevent the approval of another application if the applicant submits a Section 505(b)(1) NDA and has conducted its own adequate, well-controlled clinical trials demonstrating safety and efficacy, nor would it prevent approval of an ANDA or Section 505(b)(2) application for a product that did not incorporate the exclusivity-protected changes of the approved drug product.

Post-Approval Requirements

Any drugs for which we receive FDA approval are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse effects with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. In September 2007, the Food and Drug Administration Amendments Act of 2007 was enacted, giving the FDA enhanced post-marketing authority, including the authority to require post-marketing studies and clinical trials, labeling changes based on new safety information, and implementation of risk evaluation and mitigation strategies (“REMS”) programs, mandated by the FDA. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. Further, manufacturers of drugs must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing investment to ensure compliance. In addition, certain changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to prior FDA review and approval.

Drug manufacturers and other entities involved in the manufacturing and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. The cGMP requirements apply to all stages of the manufacturing process, including the production, processing, sterilization, packaging, labeling, storage and shipment of the drug. Manufacturers must establish validated systems to ensure that products meet specifications and regulatory standards, and test each product batch or lot prior to its release.

The FDA may restrict market availability or withdraw a product approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Discovery of previously unknown problems with a product subsequent to its approval may result in restrictions on the product or even complete withdrawal of the product from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, warning letters, holds on clinical trials, product seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal penalties.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. For example, in July 2012, FDASIA was enacted, which, among other things, expanded drug supply chain requirements

and strengthened FDA's response to drug shortages. In addition to new legislation, the FDA regulations and policies are often revised or reinterpreted by the agency in ways that may significantly affect our business and our drug candidates. It is impossible to predict whether further legislative or FDA regulation or policy changes will be enacted or implemented and what the impact of such changes, if any, may be.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

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

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our drug candidates to the extent we choose to clinically evaluate or sell any products outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country. As in the United States, post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution would apply to any product that is approved for sale outside the United States.

Third-Party Payor Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any of our drug candidates for which we obtain regulatory approval. In both the United States and foreign markets, our ability to commercialize our drug candidates successfully, and to attract commercialization partners for our drug candidates, depends in significant part on the availability of adequate financial coverage and reimbursement from third-party payors, including, in the United States, governmental payors such as the Medicare and Medicaid programs, managed care organizations, and private health insurers. Medicare is a federally funded program managed by the Centers for Medicare and Medicaid Services, or CMS, through local administrative contractors that administer coverage and reimbursement for certain healthcare items and services furnished to certain individuals aged 65 or older, disabled or suffering from end-stage renal disease. Medicaid is an insurance program for certain categories of patients whose income and assets fall below state defined levels and who are otherwise uninsured that is both federally and state funded and managed by each state. The federal government sets general guidelines for Medicaid and each state creates specific regulations that govern its individual program. Each payor has its own process and standards for determining whether it will cover and reimburse a procedure or particular product. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Therefore, achieving favorable coverage and reimbursement from government payors is usually a significant gating issue for successful introduction of a new product. The competitive position of some of our products will depend, in part, upon the extent of coverage and adequate reimbursement for such products and for the procedures in which such products are used. Prices at which we or our customers seek reimbursement for our drug candidates can be subject to challenge, reduction or denial by the government and other payors and may require us to pay rebates.

The U.S. Congress and state legislatures may, from time to time, propose and adopt initiatives aimed at cost containment, which could impact our ability to sell our drug candidates profitably. For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, which we refer to collectively as the Affordable Care Act, a sweeping law intended to

broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Affordable Care Act revised the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states once the provision is effective. Further, the law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. The Affordable Care Act also addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, and established a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. Substantial new provisions affecting compliance have also

been enacted, which may require us to modify our business practices with healthcare practitioners. We will not know the full effects of the Affordable Care Act until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the effect of the Affordable Care Act, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These automatic reductions include aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2024 unless additional Congressional action is taken. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or additional pricing pressures.

The cost of pharmaceuticals continues to generate substantial governmental and other third-party payor interest. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations and additional legislative proposals. Our results of operations could be adversely affected by current and future healthcare reforms.

Some third-party payors also require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers that use such therapies. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could have a material adverse effect on our ability to obtain adequate prices for our drug candidates and operate profitably.

Other Healthcare Laws and Compliance Requirements

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

The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the Anti-Kickback Statute to reach large settlements with healthcare companies based on sham consulting and other financial arrangements with physicians. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act. The majority of states also have anti-kickback laws which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers.

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

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

payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

There has also been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Affordable Care Act, among other things, imposes new reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug manufacturers are required to submit reports to the government by the 90th day of each subsequent calendar year. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians.

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

Employees

As of December 31, 2015, we had 46 employees, all of whom work in North Carolina, of which at least 21 hold graduate degrees (including 16 doctorate degrees) and 26 are engaged in full-time research and development activities. None of our employees are represented by a labor union, and we consider our employee relations to be good.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in 2015. Our principal executive offices are located at 4170 Mendenhall Oaks Pkwy, High Point, NC 27265, and our telephone number is (336) 841-0300.

ITEM 1A. RISK FACTORS

Risks Relating to Our Financial Position and Need for Additional Capital

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

We are a clinical-stage biopharmaceutical company with limited operating history. We have never been profitable and do not expect to be profitable in the foreseeable future. We have incurred net losses in each year since beginning to develop our drug candidates, including net losses of approximately $27.5 million, $36.1 million and $48.2 million for the years ended December 31, 2015, 2014 and 2013, respectively. As of December 31, 2015, we had a total members' deficit of approximately $196.0 million. In addition, we have not commercialized any products and have never generated any revenue from the commercialization of any product. We have devoted most of our financial resources to

research and development, including our preclinical development activities and clinical trials. We expect to incur significant additional operating losses for the next several years, at least, as we conduct our research and development activities, advance drug candidates through clinical development, complete clinical trials, seek regulatory approval and, if we receive FDA approval, commercialize our products. Furthermore, the costs of advancing drugs into each succeeding clinical phase tend to increase substantially over time. The total costs to advance any of our drug candidates to marketing approval in even a single jurisdiction would be substantial. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to begin generating revenue from the commercialization of products or achieve or maintain profitability. We expect to incur increased expenses as we continue our parallel group 18-month 800-patient Phase 3 trial of azeliragon, or the STEADFAST Study, begin outsourcing of the commercial manufacturing of azeliragon for any indications for which we receive regulatory approval, advance our other drug candidates and expand our research and development programs. Furthermore, our ability to successfully develop, commercialize and license our products and generate product revenue is subject to substantial additional risks and uncertainties, as described under "—Risks Relating to the Development and Regulatory Approval of Our Drug Candidates" and "—Risks Relating to the

Commercialization of Our Drug Candidates." As a result, we expect to continue to incur net losses and negative cash flows for the foreseeable future. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. The amount of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. In addition, we may not be able to enter into any collaborations that will generate significant cash. If we are unable to develop and commercialize one or more of our drug candidates either alone or with collaborators, or if revenues from any drug candidate that receives marketing approval are insufficient, we will not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability. If we are unable to achieve and then maintain profitability, the value of our equity securities will be materially and adversely affected.

Currently, we have no products approved for commercial sale, and to date we have not generated any revenue from product sales. As a result, our ability to generate revenue from products, curtail our losses and reach profitability is unproven, and we may never generate substantial product revenue.

We have no products approved for commercialization and have never generated any revenue from the commercialization of any product. Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize one or more of our product candidates. We do not anticipate generating revenue from product sales for a number of years. Our ability to generate future revenue from product sales depends heavily on our success in many areas, including but not limited to:

- completing research and nonclinical and clinical development of our product candidates;
- obtaining regulatory and marketing approvals for product candidates for which we complete clinical studies;
- establishing collaborations for the development of certain of our drug candidates;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and the market demand for our product candidates, if approved
- launching and commercializing product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor;
- obtaining market acceptance of our product candidates as viable treatment options
- addressing any competing technological and market developments
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- maintaining, protecting and expanding our portfolio of intellectual property rights; and
- attracting, hiring and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA or other regulatory authorities to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We will need additional capital to complete the STEADFAST Study and to complete the development and commercialization of azeliragon and our other drug candidates. If we are unable to raise sufficient capital for these purposes, we would be forced to delay, reduce or eliminate our product development programs.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We expect our research and development expenses to increase in connection with our ongoing activities, particularly as we continue the STEADFAST Study, undertake additional clinical trials of our other drug candidates and continue to work on our other research programs. Our current capital may not be sufficient for us to complete the STEADFAST Study and our planned Phase 2 trials for the clinical development of TTP399 and TTP273 and will not be sufficient for the development of our other drug candidates. As such, we may need to raise substantial additional capital to

complete the development and commercialization of azeliragon. We may fund a portion of the STEADFAST Study through licensing or other monetization of our other drug candidates, including TTP399 and TTP273. If we are unable to successfully license our other drug candidates, we may need to raise additional capital to finance the completion of the STEADFAST Study through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements.

If the FDA or other regulators require that we perform additional studies beyond those we currently expect, or if there are any delays in completing our clinical trials or the development of any of our drug candidates, our expenses could increase beyond what we currently anticipate and the timing of any potential product approval may be delayed. We have no commitments or arrangements for any additional financing to fund our research and development programs. We also will need to raise substantial additional capital in the future to complete the development and commercialization of azeliragon for additional indications and for developing our other drug candidates. Because successful development of our drug candidates is uncertain, we are unable to estimate the actual funds required to complete research and development and commercialize and license our products under development.

Until we can generate a sufficient amount of revenue from our drug candidates, if ever, we expect to finance future cash needs through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our research or development programs. We may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time. If worldwide economic conditions and the international equity and credit markets deteriorate and return to depressed states, it will be more difficult for us to obtain additional equity or credit financing, when needed.

Our future capital requirements will depend on many factors, including:

- the progress, costs, results and timing of the STEADFAST Study, and the clinical development of azeliragon;
- the willingness of the FDA to accept the STEADFAST Study, as well as our other completed and planned clinical and preclinical studies and other work, as the basis for review and approval of azeliragon;
- the outcome, costs and timing of seeking and obtaining FDA and any other regulatory approvals;
- the number and characteristics of drug candidates that we pursue, including our drug candidates in preclinical development;
- the ability of our drug candidates to progress through clinical development successfully;
- our need to expand our research and development activities;
- the costs associated with securing, establishing and maintaining commercialization capabilities;
- the costs of acquiring, licensing or investing in businesses, products, drug candidates and technologies;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- our need and ability to hire additional management and scientific and medical personnel;
- the effect of competing technological and market developments;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems; and
- the economic and other terms, timing and success of our existing licensing arrangements and any collaboration, licensing or other arrangements into which we may enter in the future.

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

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

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

We have a limited operating history and we expect a number of factors to cause our operating results to fluctuate on a quarterly and annual basis, which may make it difficult to predict our future performance.

We are a clinical stage biopharmaceutical company with a limited operating history. Our operations to date have been primarily limited to developing our technology and undertaking preclinical studies and clinical trials of azeliragon and our other drug candidates. We have not yet obtained regulatory approvals for azeliragon or any of our other drug candidates. Consequently, any statements about our future success or viability are not based on any substantial operating history or commercialized products. Our financial condition and operating results have varied significantly in the past and will continue to fluctuate from quarter-to-quarter or year-to-year due to a variety of factors, many of which are beyond our control. As a result, we may never successfully develop and commercialize a product, which could lead to a material adverse effect on the value of any investment in our securities.

Risks Relating to the Development and Regulatory Approval of Our Drug Candidates

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and failure can occur at any stage of clinical development. Because the results of earlier clinical trials are not necessarily predictive of future results, any drug candidate we advance through various stages of clinical trials or development may not have favorable results in later stages of clinical trials or development or receive regulatory approval.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any stage of clinical development. Clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical or preclinical trials. In addition, data obtained from trials are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval. For example, although treatment in our Phase 2b clinical trial in mild-to-moderate AD patients was discontinued early due to the findings of an interim futility analysis conducted approximately 12 months after all subjects were randomized, subsequent statistical analyses conducted in accordance with the protocol-specified statistical analysis plan found a statistically significant improvement, as described further under “Business—Our Alzheimer’s Program – Azeliragon—Completed Phase 2b Trial (TTP488-203).” Furthermore, an analysis of azeliragon in the subgroup of AD patients with MMSE scores of 21-26 (which are the mild AD patients that are the subjects of our Phase 3 STEADFAST Study) found that azeliragon had more pronounced efficacy in that subgroup. While we have reached an agreement with the FDA for our Phase 3 trial of azeliragon under a special protocol assessment, or SPA, there can be no assurance that the results of this Phase 3 trial will be consistent with the findings of our analyses. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a drug candidate. Frequently, drug candidates that have shown promising results in early clinical trials have subsequently suffered significant setbacks in later clinical trials. In addition, the design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. While members of our management team have experience in designing clinical trials, our company has limited experience in designing clinical trials, and we may be unable to design and execute a clinical trial to support regulatory approval. Further, clinical trials of potential products often reveal that it is not practical or feasible to continue development efforts. For example, if the results of the STEADFAST Study do not achieve the primary efficacy endpoints or demonstrate safety, the prospects for approval of azeliragon would be materially and adversely affected. If azeliragon or our other drug candidates are found to be unsafe or lack efficacy, we will not be able to obtain regulatory approval for them and our business would be harmed.

While we have negotiated a special protocol assessment, or SPA, agreement with the FDA relating to the STEADFAST Study, this agreement does not guarantee approval of azeliragon or any other particular outcome from regulatory review of the study or the drug candidate.

We have reached agreement with the FDA to conduct the STEADFAST Study, our Phase 3 trial of azeliragon pursuant to an SPA agreement. The FDA’s SPA process is designed to facilitate the FDA’s review and approval of

drugs by allowing the FDA to evaluate the proposed design and size of Phase 3 trials that are intended to form the primary basis for determining a drug product's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial design and data analysis plans, within 45 days of receipt of the request. The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the drug candidate with respect to its effectiveness against the indication studied. All agreements and disagreements between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA. Nevertheless, an SPA agreement does not guarantee approval of a drug candidate, and even if the FDA agrees to the design, execution and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, an SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor company fails to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by the sponsor in a request for the SPA change or are found to be false or omit relevant facts. In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol and such modification is

intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

In addition to the risk that the FDA may decide it is not bound by the terms of the SPA, our Phase 3 trial may not be completed in material accordance with the SPA agreement and the data generated may not meet the endpoints that have been agreed in the SPA to represent adequate evidence of effectiveness, and, for those or other reasons, may not result in any FDA approval for azeliragon. We expect that the FDA will review our compliance with the protocol under our SPA agreement and that it will conduct inspections of some of the approximately 100 sites where the clinical trial will be conducted. Each of the clinical trial sites may not pass such FDA inspections, and negative inspection results could significantly delay or prevent any potential approval for azeliragon. Even if we believe that the data collected from the Phase 3 trial demonstrate adequate evidence of efficacy in accordance with the SPA, if the FDA revokes or alters its agreement under the SPA, or if the FDA interprets the data collected from the clinical trial differently than we do, the FDA may not deem the data sufficient to support an application for regulatory approval, which could materially adversely affect our business, financial condition and results of operations.

We cannot be certain that azeliragon or any of our other drug candidates will receive regulatory approval, and without regulatory approval we will not be able to market our drug candidates and generate revenue from products. Any delay in the regulatory review or approval of azeliragon or any of our other drug candidates will materially or adversely harm our business.

We have invested a significant portion of our efforts and financial resources in the development of azeliragon, our most advanced drug candidate. Our ability to generate revenue related to product sales, which we do not expect will occur for at least the next several years, if ever, will depend on the successful development and regulatory approval of our drug candidates. We commenced the STEADFAST Study in April 2015. We may conduct the STEADFAST Study only to learn that azeliragon is not a safe or effective treatment, in which case the STEADFAST Study may not lead to regulatory approval for azeliragon. Similarly, our clinical development programs for our other drug candidates may not lead to regulatory approval from the FDA and similar foreign regulatory agencies. This failure to obtain regulatory approvals would prevent our drug candidates from being marketed and would prevent us from generating revenue from our drug candidates, which would have a material and adverse effect on our business.

All of our drug candidates require regulatory review and approval prior to commercialization, and generally, only a small percentage of pharmaceutical products under development are ultimately approved for commercial sale. Moreover, any delays in the regulatory review or approval of our drug candidates would delay market launch, increase our cash requirements and result in additional operating losses.

The process of obtaining FDA and other required regulatory approvals, including foreign approvals, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved. Furthermore, this approval process is extremely complex, expensive and uncertain, and failure to comply with applicable regulatory requirements can, among other things, result in the suspension of regulatory approval as well as possible civil and criminal sanctions. We may be unable to submit any new drug application, or an NDA, in the United States or any marketing approval application in foreign jurisdictions for any of our products. If we submit an NDA including any amended NDA or supplemental NDA, to the FDA seeking marketing approval for any of our drug candidates, the FDA must decide whether to accept or reject the submission for filing. We cannot be certain that any of these submissions will be accepted for filing and reviewed by the FDA, or that the marketing approval application submissions to any other regulatory authorities will be accepted for filing and review by those authorities. We cannot be certain that we will be able to respond to any regulatory requests during the review period in a timely manner, or at all, without delaying potential regulatory action. We also cannot be certain that any of our drug candidates will receive favorable recommendations from any FDA advisory committee or foreign regulatory bodies or be approved for marketing by the FDA or foreign regulatory authorities. In addition, delays in approvals or rejections of marketing applications may be based upon many factors, including regulatory requests for additional analyses, reports, data and studies, regulatory questions regarding data and results, changes in regulatory policy during the period of product

development and the emergence of new information regarding azeliragon or our other drug candidates.

Data obtained from preclinical studies and clinical trials are subject to different interpretations, which could delay, limit or prevent regulatory review or approval of any of our drug candidates. Furthermore, regulatory attitudes towards the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information, including on other products, policy changes and agency funding, staffing and leadership. We do not know whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects.

In addition, the environment in which our regulatory submissions may be reviewed changes over time. For example, average review times at the FDA for NDAs have fluctuated over the last ten years, and we cannot predict the review time for any of our submissions with any regulatory authorities. Review times can be affected by a variety of factors, including budget and funding levels and statutory, regulatory and policy changes. Moreover, in light of widely publicized events concerning the safety risk of certain drug products, regulatory authorities, members of the U.S. Government Accountability Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to

drug labeling that further limit use of the drug products and establishment of REMS, measures that may, for instance, place restrictions on the distribution of drug products. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to delay or terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense and a delay or failure in obtaining approval or may result in approval for a more limited indication than originally sought.

In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a drug candidate's clinical development and may vary among jurisdictions, and approval in one jurisdiction does not guarantee approval in any other jurisdiction. Our drug candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a drug candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a drug candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- the FDA or comparable foreign regulatory authorities may fail to approve the companion diagnostics we contemplate developing with partners; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our drug candidates, which would significantly harm our business, results of operations and prospects.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. For example, even if azeliragon receives regulatory approval, it may not be approved by the FDA as a disease modifying treatment. To date, the FDA has not approved any drugs for the treatment of AD as disease modifying. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

Delays in the commencement, enrollment and completion of our clinical trials could result in increased costs to us and delay or limit our ability to obtain regulatory approval for azeliragon and our other drug candidates.

Delays in the commencement, enrollment and completion of clinical trials could increase our product development costs or limit the regulatory approval of our drug candidates. We commenced the STEADFAST Study in April 2015; however, this clinical trial and reports of data from the study may not be completed on schedule, if at all. In addition, we do not know whether planned clinical trials of azeliragon in additional indications and of our other drug candidates will begin on time or will be completed on schedule or at all. The commencement, enrollment and completion of the

STEADFAST Study or other clinical trials can be delayed for a variety of reasons, including:

- inability to reach agreements on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- regulatory objections to commencing a clinical trial;
- inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indication as our drug candidates;

- withdrawal of clinical trial sites from our clinical trials as a result of changing standards of care or the ineligibility of a site to participate in our clinical trials;
- inability to obtain institutional review board, or IRB, approval to conduct a clinical trial;
- difficulty recruiting and enrolling subjects to participate in clinical trials for a variety of reasons, including willingness of subjects to undergo required study procedures, meeting the enrollment criteria for our study and competition from other clinical trial programs for the same indication as our drug candidates;
- inability to retain subjects in clinical trials due to the treatment protocol, personal issues, side effects from the therapy or lack of efficacy; and
- difficulty in importing and exporting clinical trial materials and study samples.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. Furthermore, we rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we have limited influence over their actual performance.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- failure to pass inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities;
- failure of any contract manufacturing organizations, or CMOs, that we use to comply with current Good Manufacturing Practices, or cGMPs;
- unforeseen safety issues or any determination that a clinical trial presents unacceptable health risks;
- failure to demonstrate benefit from using the drug;
- changes in the regulatory requirement and guidance; or
- lack of adequate funding to continue the clinical trial due to unforeseen costs resulting from enrollment delays, requirements to conduct additional trials and studies, increased expenses associated with the services of our CROs and other third parties or other reasons.

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

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

We have never completed a Phase 3 clinical trial or submitted an NDA before and may be unable to do so for azeliragon and other drug candidates we are developing.

We commenced the STEADFAST Study in April 2015. The conduct of Phase 3 clinical trials and the submission of a successful NDA is a complicated process. We have never conducted a Phase 3 clinical trial before, have limited experience in preparing, submitting and prosecuting regulatory filings, and have not submitted an NDA before. Consequently, we may be unable to successfully and efficiently execute and complete these planned clinical trials in a way that leads to NDA submission and approval of

azeliragon and other drug candidates we are developing. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of drug candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials would prevent or delay commercialization of azeliragon and other drug candidates we are developing.

Our drug candidates may cause serious adverse events or undesirable side effects which may delay or prevent marketing approval, or, if approval is received, require them to be taken off the market, require them to include safety warnings or otherwise limit their sales.

Serious adverse events or undesirable side effects from azeliragon or any of our other drug candidates could arise either during clinical development or, if approved, after the approved product has been marketed. The results of future clinical trials, including the STEADFAST Study, may show that our drug candidates cause serious adverse events or undesirable side effects, which could interrupt, delay or halt clinical trials, resulting in delay of, or failure to obtain, marketing approval from the FDA and other regulatory authorities or could result in a more restrictive label if our drug candidates are approved. For example, in a Phase 2 study, patients treated with azeliragon at a dose of 20 mg/day experienced a higher level of adverse events including confusion and falls, but such elevated levels of adverse events were not observed at the 5 mg/day dose.

If azeliragon or any of our other drug candidates cause serious adverse events or undesirable side effects either during clinical development, or after marketing approval, if obtained:

- regulatory authorities, IRBs, or the DSMB may impose a clinical hold, or we may decide on our own to suspend or terminate a study, which could result in substantial delays and adversely impact our ability to continue development of the product;
- regulatory authorities may require the addition of labeling statements, specific warnings, contraindications or field alerts to study subjects, investigators, physicians or pharmacies;
- we may be required to change the product design or the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we may be required to implement a REMS, which could result in substantial cost increases or signification limitations on distribution or have a negative impact on our ability to successfully commercialize the product;
- we may be required to limit the patients who can receive the product;
- we may be subject to limitations on how we promote the product;
- sales of the product may decrease significantly;
- regulatory authorities may require us to take our approved product off the market;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us from obtaining approval, or achieving or maintaining market acceptance of the affected product, if approved, or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from the sale of our products.

Azeliragon and our other drug candidates employ novel mechanisms of action and may never be approved or accepted by their intended markets.

Azeliragon and a number of our other drug candidates have novel mechanisms of action. Azeliragon targets RAGE, a novel mechanism of action for the treatment of AD. We are not aware of any other products under development that target RAGE. Our future success depends on our ability to complete the STEADFAST Study of azeliragon successfully, obtain market approval for and successfully commercialize azeliragon, as well as our ability to develop and market other drug candidates. The scientific discoveries that form the basis of our drug candidates are relatively new. We are not aware of any other drugs for the treatment of AD that have the same mechanism of action as azeliragon and even if azeliragon is approved, physicians may not be willing to use it. If we do not successfully

develop and commercialize drug candidates based upon our technological approach, we may not become profitable and the value of our common stock may decline.

Evidence of the effectiveness of azeliragon in humans is limited to data generated in a single Phase 2b study and to the group of patients in that study receiving the lower, 5 mg/day, dose of the drug. Patients in that study who received the higher, 20 mg/day, dose of the drug tended to experience adverse events. The FDA has granted Fast Track designation to our azeliragon development program based on our pre-clinical (animal) studies and not based on our Phase 2b study. The results of the Phase 2b study may not be replicated in our Phase 3 STEADFAST Study, and the FDA may not approve azeliragon for commercial use.

In addition, regulatory approval of novel drug candidates such as azeliragon and our other drug candidates using novel mechanisms of action can be more expensive and take longer than other, more well-known or extensively studied pharmaceutical or biopharmaceutical products, due to our and regulatory agencies' lack of experience with them. We are not aware of the FDA reviewing any other products targeting RAGE as a mechanism of action to date. This lack of experience may lengthen the regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these drug candidates or lead to significant post-approval limitations or restrictions.

Risks Relating to the Commercialization of Our Drug Candidates

If any of our drug candidates for which we receive regulatory approval do not achieve broad market acceptance, the revenues that are generated from their sales will be limited.

The commercial success of azeliragon and our other drug candidates, if approved, will depend upon the acceptance of these products among physicians, healthcare payors, patients and others in the medical community. The degree of market acceptance of our drug candidates will depend on a number of factors, including:

- limitations or warnings contained in a product's FDA-approved labeling;
- changes in the standard of care or the availability of alternative therapies for the targeted indications for any of our drug candidates;
- limitations in the approved indications for our drug candidates;
- demonstrated clinical safety and efficacy compared to other products;
- lack of significant adverse side effects;
- education, sales, marketing and distribution support;
- availability and degree of coverage and reimbursement from third-party payors;
- timing of market introduction and perceived effectiveness of competitive products;
- cost-effectiveness;
- availability of alternative therapies at similar or lower cost, including generics, biosimilar and over-the-counter products;
- adverse publicity about our drug candidates or favorable publicity about competitive products;
- convenience and ease of administration of our products;
- potential product liability claims; and
- government-imposed pricing restrictions.

If our drug candidates are approved, but do not achieve an adequate level of acceptance by physicians, healthcare payors, patients and others in the medical community, sufficient revenue may not be generated from these products, and we may not become or remain profitable. In addition, efforts to educate the medical community and third-party payors on the benefits of our drug candidates may require significant resources and may never be successful.

We do not have the capability to sell, distribute and market our drug candidates. If we are unable to establish an effective sales force and marketing infrastructure, or enter into acceptable third-party sales and marketing or licensing arrangements, we may not be able to commercialize our drug candidates successfully.

We do not have the capability to sell, distribute and market our drug candidates. We will need to build a commercial organization or secure a strategic partner to commercialize azeliragon and our other drug candidates. If we are unable to build a commercial infrastructure or secure a strategic collaboration, our business and results of operations will be materially and adversely affected. Development of an internal commercial organization will require substantial resources and will be time consuming. These costs may be incurred in advance of any approval of our drug candidates. In addition, we may not be able to hire a sales force in the United States that is sufficient in size or has adequate expertise in the markets that we intend to target. If we are unable to establish a sales and marketing capability, our operating results may be adversely affected. If we seek to enter into sales and marketing or licensing

arrangements with third parties for the marketing and sale of any approved products, we may be unable to enter into any such arrangements on acceptable terms, or at all.

Even if our drug candidates receive regulatory approval, we will still be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense, and we may still face future development and regulatory difficulties.

Even if regulatory approval is obtained for any of our drug candidates, regulatory authorities may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. Given the number of high profile adverse safety events with certain drug products, regulatory authorities may require, as a condition of approval, costly REMS, which may include safety surveillance, restricted distribution and use, patient education, enhanced labeling, expedited reporting of certain adverse events, pre-approval of promotional materials and restrictions on direct-to-consumer advertising. For example, any labeling approved for any of our drug candidates may include a restriction on the term of its use, or it may not include one or more of our intended indications or patient populations. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs during the period of product development, clinical trials and regulatory review and approval, as well as increased costs to assure compliance with any new post-approval regulatory requirements.

Our drug candidates will also be subject to ongoing regulatory requirements for the labeling, packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information. In addition, sellers of approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMP. As such, we and our CMOs are subject to continual review and periodic inspections to assess compliance with cGMP and the terms and conditions of approvals. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with certain requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have approval.

If a regulatory agency discovers problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or objects to the promotion, marketing or labeling of a product, it may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If our drug candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- mandate modifications to promotional materials or require us to disseminate corrective information to healthcare practitioners or other parties;
- require us to enter into a consent decree or permanent injunction, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- impose other civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications filed by us;
- impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or require a product recall.

The FDA's policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We expect that our existing and future drug candidates will face competition, and most of our competitors have significantly greater resources than we do.

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical companies, generic or biosimilar drug companies, universities and other research institutions. Our drug candidates, if successfully developed and approved, will compete in crowded and competitive markets. In order to compete with approved products, our drug candidates will need to demonstrate compelling advantages. We believe the key competitive factors that will affect the development and commercial success of our drug candidates are efficacy, safety and tolerability profile, mechanism of action, control and predictability, convenience of dosing and price and reimbursement. Our most advanced drug candidate, azeliragon, is being developed for use in the treatment of patients with mild AD

receiving a standard of care with an aceytlcholinesterase inhibitor and/or memantine. If approved for this indication, new competitors may emerge and azeliragon may face competition from several therapies currently in clinical development that address different mechanisms of action than azeliragon. Potential competitors with products in late stage clinical development are Eli Lilly and Company, with its drug candidates solanezumab and gantenerumab, and Merck & Co., with its drug candidate MK-8931. Our drug candidates TTP399 and TTP273, compounds for treating type 2 diabetes, would compete with both currently available non-insulin medication products and marketed non-insulin anti-diabetic agents that are in clinical development. Competition is high among novel drug classes for the treatment of type 2 diabetes. Products that are currently available that may compete with TTP399 and TTP273 include DPP-4 inhibitors, such as sitagliptin or saxagliptin, and SGLT-2 inhibitors, such as dapagliflozin and canagliflozin. Companies with GKAs in early clinical development that may compete with TTP399 include Advinus Therapeutics Ltd., Eli Lilly and Company, Pfizer Inc., Hua Medicine Ltd. and Teijin Pharma Limited. TTP273 would face competition from GLP-1r agonists that are being developed and are currently available, including Trulicity, which is marketed by Eli Lilly and Company, Tanzeum, which is marketed by GlaxoSmithKline plc, Bydureon, which is marketed by AstraZeneca plc, and Victoza, which is marketed by Novo Nordisk A/S.

Many of our potential competitors have substantially greater:

·resources, including capital, personnel and technology;
·research and development capability;
·clinical trial expertise;
·regulatory expertise;
·intellectual property rights, including patent rights;
·expertise in obtaining, maintaining, defending and enforcing intellectual property rights, including patent rights;
·manufacturing and distribution expertise; and
·sales and marketing expertise.

In addition, academic and government institutions are increasingly likely to enter into exclusive licensing agreements with commercial enterprises, including our competitors, to market commercial products based on technology developed at such institutions. Many of these competitors have significant products approved or in development that could be competitive with our products.

Accordingly, our competitors may be more successful than us in obtaining regulatory approval for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, less costly, or more effectively marketed and sold, than any drug candidate we may commercialize and may render our drug candidates obsolete or non-competitive before we can recover the expenses of their development and commercialization. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. Finally, the development of new treatment methods for the diseases we are targeting could render our drug candidates non-competitive or obsolete.

Healthcare cost containment initiatives and the growth of managed care may limit our revenues and profitability.

Our ability to commercialize our products successfully may be negatively affected by the ongoing efforts of governmental and third-party payors to contain the cost of health care. In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Affordable Care Act, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and established a new Medicare Part D coverage gap discount

program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These automatic reductions include aggregate reductions of Medicare payments to providers of 2% per

fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2024 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or additional pricing pressures.

Both governmental and third-party payers are challenging the cost of healthcare products and services, denying or limiting coverage and reimbursement amounts for new therapeutic products, for FDA-approved products considered experimental or investigational or used for disease indications without FDA marketing approval. Any restrictions in coverage or reductions in reimbursement rates under government programs often result in reductions in reimbursement rates by insurance companies and other third-party payors.

Even if we succeed in bringing azeliragon or any of our other drug candidates to the market, we may not be considered cost-effective, and governmental or third-party payor coverage and reimbursement might not be available or sufficient. If adequate governmental or third-party coverage or reimbursement is not available, we may not be able to maintain price levels sufficient to realize an appropriate return on our investment in research and product development. In addition, legislation and regulations affecting the pricing of pharmaceuticals may change in ways adverse to us before or after any of our proposed products are approved for marketing.

Therefore, adverse changes in third-party payor coverage and reimbursement and/or new state and federal healthcare reform measures that may be adopted in the future could have a material adverse effect on our businesses, financial conditions and results of operations.

Our current and future relationships with healthcare professionals, principal investigators, consultants, customers (actual and potential) and third-party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable healthcare laws and regulations.

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any drug candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers (actual and potential) and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws, including, without limitation:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation. In addition, the Affordable Care Act provided that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- federal civil and criminal false claims laws, including the federal False Claims Act, which impose criminal and civil penalties, including civil whistleblower actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the civil monetary penalties statute, which imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose obligations on covered entities, including healthcare providers, health plans, and healthcare clearinghouses, as well as their respective business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act and its implementing regulations, which imposed annual reporting requirements for certain manufacturers of drugs, devices, biologicals and medical supplies for payments and "transfers of value" provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our future business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business activities, including our relationships with physician consultants, some of whom may prescribe our product candidates, if approved, in the future, may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, which could significantly harm our business.

If we try to obtain approval to commercialize any products outside the United States, many of the same risks that apply to obtaining approvals in the United States will likely apply to such a process, and even if we obtain approval to commercialize any such products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If we try to obtain approval to commercialize any of our products outside the United States, many of the same risks with respect to obtaining such approvals in the United States will apply to that process. If azeliragon or any of our other drug candidates are approved for commercialization outside of the United States, we intend to enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. In that event, we expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals;
- reduced protection for intellectual property rights, including trade secret and patent rights;
- existing tariffs, trade barriers and regulatory requirements and expected or unexpected changes;
- economic weakness, including inflation, or political instability in foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more or less common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
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business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, hurricanes, floods and fires; and

- difficulty in importing and exporting clinical trial materials and study samples.

Our business and operations would suffer in the event of computer system failures, cyber-attacks or a deficiency in our cyber-security.

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber-intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Also, confidential patient and other information may be compromised in a cyber-attack or cyber-intrusion. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur material legal claims and liability, damage to our reputation, and the further development of our drug candidates could be delayed.

Risks Relating to Our Dependence on Third Parties

We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize our drug candidates successfully, if at all.

We intend to seek collaborative relationships for the development and commercialization of our drug candidates, including azeliragon. Failure to obtain a collaborative relationship for azeliragon, particularly in the European Union and for other markets requiring extensive sales efforts, may significantly impair the potential for this drug candidate. We also will need to enter into collaborative relationships to provide funding to support our other research and development programs. The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty, including:

- a collaboration partner may shift its priorities and resources away from our drug candidates due to a change in business strategies, or a merger, acquisition, sale or downsizing;
- a collaboration partner may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- a collaboration partner may cease development in therapeutic areas which are the subject of our strategic collaboration;
- a collaboration partner may not devote sufficient capital or resources towards our drug candidates;
- a collaboration partner may change the success criteria for a drug candidate thereby delaying or ceasing development of such candidate;
- a significant delay in initiation of certain development activities by a collaboration partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- a collaboration partner could develop a product that competes, either directly or indirectly, with our drug candidate;
- a collaboration partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- a collaboration partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- a partner may exercise a contractual right to terminate a strategic alliance;
- a dispute may arise between us and a partner concerning the research, development or commercialization of a drug candidate resulting in a delay in milestones, royalty payments or termination of an alliance and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and
- a partner may use our products or technology in such a way as to invite litigation from a third party.

For example, we previously licensed the development of azeliragon to Pfizer Inc. in 2006, before Pfizer determined not to pursue the development of the program and we reacquired azeliragon in 2011, and Forest Laboratories had previously licensed our GKA programs, including TTP399, but decided to return the GKA programs to us in 2013, shortly before its acquisition by Actavis plc. Any collaborative partners we enter into agreements with in the future may also shift their priorities and resources away from our drug candidates or seek to renegotiate or terminate their relationships with us.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing or commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our drug candidates, undertake development and commercialization activities at our own expense or find alternative sources of capital.

We rely on third parties to conduct, supervise and monitor certain of our clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We rely on contract research organizations ("CROs") and clinical trial sites to ensure the proper and timely conduct of certain of our clinical trials, including the STEADFAST Study. While we have agreements governing their activities, we will have limited influence over their actual performance. We will control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that our clinical trials are conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with the FDA's good clinical practices requirements, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCPs. In addition, our clinical trials conducted by third parties will require a sufficiently large number of test subjects to evaluate the safety and effectiveness of a drug candidate. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, our clinical trials may be delayed or we may be required to repeat such clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and we are not able to control whether or not they devote sufficient time and resources to our clinical trials. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our drug candidates. As a result, our financial results and the commercial prospects for such drug candidates would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

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

We do not have multiple sources of supply for the components used in azeliragon and our other drug candidates. If we were to lose a supplier, it could have a material adverse effect on our ability to complete the development of azeliragon or our other drug candidates. If we obtain regulatory approval for azeliragon or our other drug candidates we would need to expand the supply of its components in order to commercialize them.

We do not have multiple sources of supply for the components used in azeliragon and our other drug candidates. We also do not have long-term supply agreements with any of our suppliers. We are currently evaluating drug manufacturers that will produce the commercial supply of both the drug substance and drug product of azeliragon. It is our expectation that only one supplier of drug substance and one supplier of product will be qualified as vendors with the FDA. If for any reason we are unable to obtain drug substance or drug product from the manufacturers we select, we would have to seek to obtain these from other manufacturers. We may not be able to establish additional sources of supply for our drug candidates, or may be unable to do so on acceptable terms. Such suppliers are subject to regulatory requirements, covering manufacturing, testing, quality control and record keeping relating to our drug candidates and subject to ongoing inspections by the regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in long delays and interruptions.

The number of suppliers of the raw material components of our drug candidates is limited. In the event it is necessary or desirable to acquire supplies from an alternative supplier, we might not be able to obtain them on commercially reasonable terms, if at all. It could also require significant time and expense to redesign our manufacturing processes to work with another company.

As part of any marketing approval, a manufacturer and its processes are required to be qualified by the FDA prior to commercialization. If supply from the approved supplier is interrupted, there could be a significant disruption in commercial supply. An alternative vendor would need to be qualified through an NDA amendment or supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new supplier is relied upon for commercial production. Switching vendors may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

If we are unable to obtain the supplies we need at a reasonable price or on a timely basis, it could have a material adverse effect on our ability to complete the development of azeliragon and our other drug candidates or, if we obtain regulatory approval for azeliragon or our other drug candidates, to commercialize them.

We intend to rely on third-party manufacturers to produce our drug candidates. If we experience problems with any of these suppliers, the manufacturing of our drug candidates or products could be delayed.

We do not have the capability to manufacture our drug candidates and do not intend to develop that capability. In order to continue to develop our drug candidates, apply for regulatory approvals and ultimately commercialize products, we need to develop, contract for or otherwise arrange for the necessary manufacturing capabilities. The facilities used by our CMOs to manufacture our drug candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements, known as cGMPs, for manufacture of both active drug substances and finished drug products. If our CMOs cannot successfully manufacture material that conforms to our specifications and the regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drug candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our drug candidates, if approved.

In addition, there are a limited number of manufacturers that operate under the FDA's cGMP regulations capable of manufacturing our drug candidates. As a result, we may have difficulty finding manufacturers for our drug candidates with adequate capacity for our needs. If we are unable to arrange for third-party manufacturing of our drug candidates on a timely basis, or to do so on commercially reasonable terms, we may not be able to complete development of our drug candidates or market them.

Reliance on third-party manufacturers entails risks to which we might not be subject if we manufactured drug candidates ourselves, including:

- the limited number of manufacturers that could produce our drug candidates for us
- the inability to meet our product specifications and quality requirements consistently;
- inability to access production facilities on a timely basis;
- inability or delay in increasing manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for commercial level activity;
- a failure to satisfy the FDA's cGMP requirements and similar foreign standards on a consistent basis;
- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a single sources of supply which, if unavailable, would delay our ability to complete our clinical trials or to sell any product for which we have received marketing approval;

- the lack of qualified backup suppliers for supplies that are currently purchased from a single source supplier;
- carrier disruptions or increased costs that are beyond our control; and
- the failure to deliver products under specified storage conditions and in a timely manner.

Any of these risks could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our products, cause us to incur higher costs and prevent us from commercializing our drug candidates successfully. Manufacturing of

our drug candidates and any approved products could be disrupted or halted if our third-party manufacturers do not comply with cGMP or foreign manufacturing standards, even if the compliance failure does not relate to our drug candidates or approved products. Furthermore, if any of our drug candidates are approved and our third-party manufacturers fail to deliver the required commercial quantities of finished product on a timely basis and at commercially reasonable prices and we are unable to find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volumes and quality and on a timely basis, we would likely be unable to meet demand for our products and could lose potential revenue. It may take several years to establish an alternative source of supply for our drug candidates and to have any such new source approved by the FDA or a foreign regulator.

Risks Relating to Our Intellectual Property

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

Our commercial success will depend in part on our ability to:

·apply for, obtain, maintain and enforce patents;
·protect trade secrets; and
·operate without infringing upon the proprietary rights of others.

We will be able to protect our proprietary technology from unauthorized use by third parties only to the extent that such proprietary rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. Any non-confidential disclosure to or misappropriation by third parties of our confidential or proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

As of December 31, 2015, we were the owner of record of at least 56 issued U.S. patents and at least 225 issued non-U.S. patents, as well as the licensee of at least 12 issued U.S. patents and at least 59 issued non-U.S. patents. As of December 31, 2015, we were actively pursuing 19 U.S. patent applications, of which two are provisional and 17 are non-provisional, two international patent applications and at least 146 non-U.S. patent applications in twelve or more jurisdictions as the owner of record, in addition to at least two non-U.S. patent applications under license.

The patent application process, also known as patent prosecution, is expensive and time-consuming, and we and our current or future licensors and licensees may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our current licensors, or any future licensors or licensees, will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, these and any of our patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims or inventorship. If we or our current licensors or licensees, or any future licensors or licensees, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our current licensors or licensees, or any future licensors or licensees, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Any of these outcomes could impair our ability to prevent competition from third parties, which may harm our business.

The patent applications that we own or license may fail to result in issued patents in the United States or in other countries. Even if patents do issue on such patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. For example, U.S. patents can be challenged by any person before the new USPTO Patent Trial and Appeals Board at any time within the one year period following that person’s receipt of an allegation of infringement of the patents. Patents

granted by the European Patent Office may be similarly opposed by any person within nine months from the publication of the grant. Similar proceedings are available in other jurisdictions, and in the United States, Europe and other jurisdictions third parties can raise questions of validity with a patent office even before a patent has granted. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is successfully challenged, then our ability to commercialize such product candidates could be negatively affected, and we may face unexpected competition that could harm our business. Further, if we encounter delays in our clinical trials, the period of time during which we or our collaborators could market our product candidates under patent protection would be reduced.

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

- we might not have been the first to invent or the first to file the inventions covered by each of our pending patent applications and issued patents;
- others may be able to make, use, sell, offer to sell or import products that are similar to our products or product candidates but that are not covered by the claims of our patents; others may independently develop similar or alternative technologies or duplicate any of our technologies;
- the proprietary rights of others may have an adverse effect on our business;
- any proprietary rights we do obtain may not encompass commercially viable products, may not provide us with any competitive advantages or may be challenged by third parties;
- any patents we obtain or our in-licensed issued patents may not be valid or enforceable; or
- we may not develop additional technologies or products that are patentable or suitable to maintain as trade secrets.

If we or our current licensors or licensees, or any future licensors or licensees, fail to prosecute, maintain and enforce patent protection for our product candidates, our ability to develop and commercialize our product candidates could be harmed and we might not be able to prevent competitors from making, using and selling competing products. This failure to properly protect the intellectual property rights relating to our product candidates could harm our business, financial condition and operating results. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

Even where laws provide protection, costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and the outcome of such litigation would be uncertain. If we or one of our collaborators were to initiate legal proceedings against a third party to enforce a patent covering the product candidate, the defendant could assert an affirmative defense or counterclaim that our patent is not infringed, invalid and/or unenforceable. In patent litigation in the United States, defendant defenses and counterclaims alleging noninfringement, invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, anticipation or obviousness, and lack of written description, definiteness or enablement. Patents may be unenforceable if someone connected with prosecution of the patent withheld material information from the USPTO, or made a misleading statement, during prosecution. The outcomes of proceedings involving assertions of invalidity and unenforceability are unpredictable. It is possible that prior art of which we and the patent examiner were unaware during prosecution exists, which would render our patents invalid. Moreover, it is also possible that prior art may exist that we are aware of, but that we do not believe are relevant to our current or future patents, that could nevertheless be determined to render our patents invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability of our patents covering one of our product candidates, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would harm our business. Moreover, our competitors could counterclaim in any suit to enforce our patents that we infringe their intellectual property. Furthermore, some of our competitors have substantially greater intellectual property portfolios, and resources, than we do.

Our ability to stop third parties from using our technology or making, using, selling, offering to sell or importing our products is dependent upon the extent to which we have rights under valid and enforceable patents that cover these activities. If any patent we currently or in the future may own or license is deemed not infringed, invalid or unenforceable, it could impact our commercial success. We cannot predict the breadth of claims that may be issued from any patent applications we currently or may in the future own or license from third parties.

To the extent that consultants or key employees apply technological information independently developed by them or by others to our product candidates, disputes may arise as to who has the proprietary rights to such information and product candidates, and certain of such disputes may not be resolved in our favor. Consultants and key employees that work with our confidential and proprietary technologies are required to assign all intellectual property rights in their inventions and discoveries created during the scope of their work to our company. However, these consultants or key

employees may terminate their relationship with us, and we cannot preclude them indefinitely from dealing with our competitors.

If we are unable to prevent disclosure of our trade secrets or other confidential information to third parties, our competitive position may be impaired.

We also may rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. Our ability to stop third parties from obtaining the information or know-how necessary to make, use, sell, offer to sell or import our products or practice our technology is dependent in part upon the extent to which we prevent disclosure of the trade secrets that cover these activities. Trade secret rights can be lost through disclosure to third parties. Although we use reasonable efforts to

protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our trade secrets to third parties, resulting in loss of trade secret protection. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how, which would not constitute a violation of our trade secret rights. Enforcing a claim that a third party is engaged in the unlawful use of our trade secrets is expensive, difficult and time consuming, and the outcome is unpredictable. In addition, recognition of rights in trade secrets and a willingness to enforce trade secrets differs in certain jurisdictions.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a “first to file” system. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our or our collaborators’ patent applications and the enforcement or defense of our or our collaborators’ issued patents, all of which could harm our business, results of operations and financial condition.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation could harm our business.

Our commercial success depends significantly on our ability to operate without infringing, violating or misappropriating the patents and other proprietary rights of third parties. Our own technologies may infringe, violate or misappropriate the patents or other proprietary rights of third parties, or we may be subject to third-party claims of such infringement. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties, exist in the fields in which we are developing our product candidates. Because some patent applications may be maintained in secrecy until the patents are issued, because publication of patent applications is often delayed, and because publications in the scientific literature often lag behind actual discoveries, we cannot be certain that we were the first to invent the technology or that others have not filed patent applications for technology covered by our pending applications. We may not be aware of patents that have already issued that a third party might assert are infringed by our product candidates. It is also possible that patents of which we are aware, but which we do not believe are relevant to our product candidates, could nevertheless be found to be infringed by our product candidates. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect. In the future, we may agree to indemnify our manufacturing partners against certain intellectual property claims brought by third parties.

Intellectual property litigation involves many risks and uncertainties, and there is no assurance that we will prevail in any lawsuit brought against us. Third parties making claims against us for infringement, violation or misappropriation of their intellectual property rights may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Further, if a patent infringement suit were brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. Defense of these claims, regardless of their merit, would cause us to incur substantial expenses and, would be a substantial diversion of resources from our business. In the event of a successful claim of any such infringement, violation or misappropriation, we may need to obtain licenses from such third parties and we and our partners may be prevented from pursuing product development or commercialization and/or may be required to pay damages. We cannot be certain that any licenses required under such patents or proprietary rights would be made available to us, or that any offer to license would be made available to us on commercially reasonable terms. If we cannot obtain such licenses, we and our collaborators may be restricted or prevented from manufacturing and selling products employing our

technology. These adverse results, if they occur, could adversely affect our business, results of operations and prospects, and the value of our shares.

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

The biotechnology and pharmaceutical industries have been characterized by extensive litigation regarding patents and other intellectual property rights. The defense and prosecution of contractual or intellectual property lawsuits, USPTO interference or derivation proceedings, European Patent Office oppositions and related legal and administrative proceedings in the United States, Europe and other countries, involve complex legal and factual questions. As a result, such proceedings may be costly and time-consuming to pursue and their outcome is uncertain.

Litigation may be necessary to:

- protect and enforce our patents and any future patents issuing on our patent applications;
- enforce or clarify the terms of the licenses we have granted or may be granted in the future;
- protect and enforce trade secrets, know-how and other proprietary rights that we own or have licensed, or may license in the future; or
- determine the enforceability, scope and validity of the proprietary rights of third parties and defend against alleged patent infringement.

Competitors may infringe our intellectual property. As a result, we may be required to file infringement claims to stop third-party infringement or unauthorized use. This can be expensive, particularly for a company of our size, and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patent claims do not cover its technology or that the factors necessary to grant an injunction against an infringer are not satisfied. An adverse determination of any litigation or other proceedings could put one or more of our patents at risk of being invalidated, interpreted narrowly, or amended such that they do not cover our product candidates. Moreover, such adverse determinations could put our patent applications at risk of not issuing, or issuing with limited and potentially inadequate scope to cover our product candidates or to prevent others from marketing similar products.

Interference, derivation or other proceedings brought at the USPTO, may be necessary to determine the priority or patentability of inventions with respect to our patent applications or those of our licensors or potential collaborators. Litigation or USPTO proceedings brought by us may fail or may be invoked against us by third parties. Even if we are successful, domestic or foreign litigation or USPTO or foreign patent office proceedings may result in substantial costs and distraction to our management. We may not be able, alone or with our licensors or potential collaborators, to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other proceedings, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. In addition, during the course of this kind of litigation or proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

Some of our competitors may be able to sustain the costs of patent-related disputes, including patent litigation, more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

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

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States do not afford intellectual property protection to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory

licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

If we do not obtain patent term extensions for our drug candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of our drug candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Act. The Hatch-Waxman Act permits a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension, and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. For example, patents providing intellectual property protection for azeliragon are scheduled to expire in 2023, but if we obtain the maximum possible extension in the United States, a period of patent extension for the approved azeliragon product could extend into 2029. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the original expiration dates of our patents, and our business may be materially harmed.

Risks Relating to Employee Matters and Managing Growth

We will need to expand our operations and increase the size of our company, and we may experience difficulties in managing growth.

As we advance our drug candidates through preclinical studies and clinical trials and develop new drug candidates, we will need to increase our product development, scientific and administrative headcount to manage these programs. If we commercialize our products, we will be required to expand our staff further, particularly in sales and marketing. See "—Risks Relating to the Commercialization of Our Drug Candidates." We do not have the capability to sell, distribute and market our drug candidates. If we are unable to establish an effective sales force and marketing infrastructure, or enter into acceptable third-party sales and marketing or licensing arrangements, we may not be able to commercialize our drug candidates successfully. In addition, to meet our obligations as a public company, we will need to increase our general and administrative capabilities. Our management, personnel and systems currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and various projects requires that we:

- successfully attract and recruit new employees with the expertise and experience we will require;
- manage our clinical programs effectively, which we anticipate being conducted at numerous clinical sites;
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develop a marketing, distribution and sales infrastructure if we seek to market our products directly; and

- continue to improve our operational, manufacturing, financial and management controls, reporting systems and procedures.

If we are unable to successfully manage this growth and increased complexity of operations, our business may be adversely affected.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel.

We may not be able to attract or retain qualified management, finance, scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of our executive officers and key employees. If we lose one or more of our executive officers or key personnel, our ability to implement our business strategy successfully could be seriously harmed. Any of our executive officers or key employees may terminate their employment at any time. Replacing executive officers and key employees may be difficult, will be costly and may take an extended period of time because of the limited number of individuals in our industry with the mix of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel. Our failure to attract and retain key personnel could materially harm our business.

Failure to build our finance infrastructure and improve our accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies.

As a public company, we will operate in an increasingly demanding regulatory environment, which requires us to comply with applicable provisions of the Sarbanes-Oxley Act of 2002 and the related rules and regulations of the Securities and Exchange Commission, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes-Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud.

We will need to hire additional finance personnel and build our financial infrastructure as we transition to operating as a public company, including complying with the applicable requirements of Section 404 of the Sarbanes-Oxley Act. We may be unable to do so on a timely basis.

Until we are able to expand our finance and administrative capabilities and establish necessary financial reporting infrastructure, we may not be able to prepare and disclose, in a timely manner, our financial statements and other required disclosures or comply with the applicable provisions of the Sarbanes-Oxley Act or existing or new reporting requirements. If we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed and investors could lose confidence in our reported financial information.

Our employees, independent contractors, principal investigators, CROs, consultants and collaborators may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and collaborators may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate the regulations of the FDA and non-U.S. regulators, including those laws requiring the reporting of true, complete and accurate information to the FDA and non-U.S. regulators, healthcare fraud and abuse laws and regulations in the United States and abroad, or laws that require the reporting of true and accurate financial information and data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. These activities also include the improper use or disclosure of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant

impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

Other Risks Relating to Our Business

We may use our financial and human resources to pursue a particular research program or drug candidate and fail to capitalize on programs or drug candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and human resources, we intend to focus primarily on the regulatory approval of azeliragon, including the completion of the STEADFAST Study. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on existing and future drug candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial

potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through strategic alliance, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate, or we may allocate internal resources to a drug candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of any future products we develop.

We face an inherent risk of product liability as a result of the clinical testing of our drug candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for azeliragon or any future drug candidates or products we develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants or cancellation of clinical trials;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- the inability to commercialize any products we develop; and
- a decline in our share price.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of azeliragon or any future products we develop. We currently carry clinical trial liability insurance in the amount of $10.0 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. If and when we obtain approval for marketing azeliragon, we intend to expand our insurance coverage to include the sale of azeliragon, however, we may be unable to obtain this liability insurance on commercially reasonable terms.

Our operations involve hazardous materials, which could subject us to significant liabilities.

Our research and development processes involve the controlled use of hazardous materials, including medical waste. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge or injury from these materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of these materials. We could be subject to civil damages in the event of exposure of individuals to hazardous materials. In addition, claimants may sue us for injury or contamination that results from our use of these materials and our liability may exceed our total assets. We have general liability and umbrella insurance of up to $6.0 million per occurrence, with an annual aggregate limit of $7.0 million, which excludes pollution liability.

This coverage may not be adequate to cover all claims related to our hazardous materials. Furthermore, if we were to be held liable for a claim involving hazardous materials, this liability could exceed our insurance coverage, if any, and our other financial resources. Compliance with environmental and other laws and regulations may be expensive and current or future regulations may impair our research, development or production efforts.

Our insurance policies are expensive and protect us only from some business risks, which will leave us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, auto, workers' compensation, umbrella, clinical trial and directors' and officers' insurance. We also expect that operating as a public company will make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our Board of Directors, our board committees or as executive officers. We do not know, however, if we will be able to maintain existing insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash position and results of operations.

The market for our proposed products is rapidly changing and competitive, and new drugs and new treatments that may be developed by others could impair our ability to maintain and grow our businesses and remain competitive.

The pharmaceutical and biotechnology industries are subject to rapid and substantial technological change. Developments by others may render proposed products noncompetitive or obsolete, or we may be unable to keep pace with technological developments or other market factors. Technological competition from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase.

As a company with nominal revenues engaged in the development of drug technologies, our resources are limited, and we may experience technical challenges inherent in such technologies. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competition. Some of these technologies may have an entirely different approach or means of accomplishing similar therapeutic effects compared to our proposed products. Our competitors may develop drugs that are safer, more effective or less costly than our proposed products and, therefore, present a serious competitive threat to us.

The potential widespread acceptance of therapies that are alternatives to those of ours may limit market acceptance of our drug candidates, even if commercialized. Some of our targeted diseases and conditions can also be treated by other medication. These treatments may be widely accepted in medical communities and have a longer history of use. The established use of these competitive drugs may limit the potential for our technologies, formulations and products to receive widespread acceptance if commercialized.

Therefore, changes in the market for our products and the availability of new or alternative treatments could have a material adverse effect on our businesses, financial conditions and results of operations.

Risks Related to our Common Stock

MacAndrews & Forbes Incorporated ("MacAndrews") has substantial influence over our business, and their interests may differ from our interests or those of our other stockholders.

MacAndrews holds, directly or indirectly, a majority of our combined voting power. Due to its ownership and rights under our investor rights agreement, amended and restated certificate of incorporation and amended and restated bylaws, MacAndrews has the power to control us and our subsidiaries, including the power to:

- nominate a majority of our directors, elect a majority of our directors and appoint our executive officers, set our management policies and exercise overall control over our company and subsidiaries;
- determine the composition of the committees on our Board of Directors;
- agree to sell or otherwise transfer a controlling stake in our company; and

- determine the outcome of substantially all actions requiring stockholder approval, including transactions with related parties, corporate reorganizations, acquisitions and dispositions of assets and dividends.

The interests of MacAndrews may differ from our interests or those of our other stockholders and the concentration of control in MacAndrews will limit other stockholders' ability to influence corporate matters. The concentration of ownership and voting power with MacAndrews may also delay, defer or even prevent an acquisition by a third party or other change of control of our company and may make some transactions more difficult or impossible without the support of MacAndrews, even if such events are in the best interests of our other stockholders. The concentration of voting power with MacAndrews may have an adverse effect on the price of our Class A common stock. Our company may take actions that our other stockholders do not view as beneficial, which may adversely affect our results of operations and financial condition and cause the value of our Class A common stock to decline.

Our directors who have relationships with MacAndrews may have conflicts of interest with respect to matters involving our company.

The majority of our directors are affiliated with MacAndrews. These persons will have fiduciary duties to us and in addition will have duties to MacAndrews. In addition, our amended and restated certificate of incorporation provides that none of MacAndrews, any of our non-employee directors who are employees, affiliates or consultants of MacAndrews or its affiliates (other than us or our subsidiaries) or any of their respective affiliates will be liable to us or our stockholders for breach of any fiduciary duty by reason of the fact that any such individual directs a corporate opportunity to MacAndrews or its affiliates instead of us, or does not communicate information regarding a corporate opportunity to us that such person or affiliate has directed to MacAndrews or its affiliates. As a result, such circumstances may entail real or apparent conflicts of interest with respect to matters affecting both us and MacAndrews, whose interests, in some circumstances, may be adverse to ours. In addition, as a result of MacAndrews' indirect ownership interest, conflicts of interest could arise with respect to transactions involving business dealings between us and MacAndrews or their affiliates, including potential business transactions, potential acquisitions of businesses or properties, the issuance of additional securities, the payment of dividends by us and other matters.

We do not anticipate paying cash dividends on our Class A common stock, and accordingly, stockholders must rely on stock appreciation for any return on their investment.

We have never declared or paid any cash dividend on our Class A common stock and do not anticipate paying cash dividends on our Class A common stock in the future. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, the only return to stockholders will be appreciation in the price of our Class A common stock, which may never occur. Investors seeking cash dividends should not invest in our Class A common stock.

Our share price may be volatile, which could subject us to securities class action litigation and result in substantial losses for our stockholders.

The market price of shares of our Class A common stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- results and timing of our clinical trials and receipt of data from the trials;
- results of clinical trials of our competitors' products;
- failure or discontinuation of any of our research programs;
- delays in the development or commercialization of our potential products;
- regulatory actions with respect to our products or our competitors' products;
- actual or anticipated fluctuations in our financial condition and operating results;
- actual or anticipated changes in our growth rate relative to our competitors;
- actual or anticipated fluctuations in our competitors' operating results or changes in their growth rate;
- competition from existing products or new products that may emerge;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- issuance of new or updated research or reports by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- additions or departures of key management or scientific personnel;
- disputes or other developments related to proprietary rights, including patents, litigation matters and our ability to obtain, maintain, defend or enforce proprietary rights relating to our products and technologies;
- announcement or expectation of additional financing efforts;

- sales of our Class A common stock by us, our insiders or our other stockholders;
- issues in manufacturing our potential products;
- market acceptance of our potential products;

·market conditions for biopharmaceutical stocks in general; and
·general economic and market conditions.

Furthermore, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These broad market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations, may negatively impact the market price of shares of our Class A common stock. In addition, such fluctuations could subject us to securities class action litigation, which could result in substantial costs and divert our management's attention from other business concerns, which could potentially harm our business. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price at which they purchased their shares.

An active trading market for our Class A common stock may not be sustained.

Our shares of Class A common stock began trading on The NASDAQ Global Market on July 30, 2015. Given the limited trading history of our Class A common stock, there is a risk that an active trading market for our shares will not be sustained, which could put downward pressure on the market price of our Class A common stock and thereby affect the ability of our stockholders to sell their shares.

The trading market for our Class A common stock will be influenced by the research and reports that equity research analysts publish about us and our business.

The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

A substantial portion of our total outstanding shares may be sold into the market at any time. This could cause the market price of our Class A common stock to drop significantly, even if our business is doing well.

The market price of our Class A common stock could decline as a result of sales of a large number of shares of our Class A common stock or the perception that such sales could occur. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and price that we deem appropriate.

As of December 31, 2015, MacAndrews and its affiliates hold 23,059,232 non-voting common units of vTv LLC ("vTv Units") and the same number of shares of vTv Therapeutics Inc. Class B common stock as well as an aggregate of 1,915,666 shares of our Class A common stock. As a result, MacAndrews and its affiliates hold shares representing approximately 76.1% of the combined voting power of our outstanding common stock. Pursuant to the terms of the Exchange Agreement among the Company, vTv LLC and the holders of vTv Units party thereto (the "Exchange Agreement"), vTv Units (along with the corresponding number of shares of our Class B common stock) will be exchangeable for (i) shares of our Class A common stock on a one-for-one basis or (ii) cash (based on the market price of the shares of Class A common stock), at our option (as the managing member of vTv Therapeutics LLC). Shares of our Class A common stock issuable upon an exchange of vTv Units as described above would be considered "restricted securities," as that term is defined in Rule 144 under the Securities Act, unless the exchange is registered under the Securities Act.

In addition, on August 13, 2015, we filed a registration statement under the Securities Act registering 3,250,000 shares of our Class A common stock reserved for issuance under our 2015 Plan, and we have entered into an investor rights

agreement with an affiliate of MacAndrews providing certain governance and registration rights.

Future sales and issuances of our Class A common stock or rights to purchase Class A common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell Class A common stock, convertible securities or other equity securities. If we sell Class A common stock, convertible securities or other equity securities, the percentage ownership of our stockholders will be diluted. In addition, new investors could gain rights superior to our existing stockholders.

We are an “emerging growth company,” and are taking advantage of reduced disclosure requirements applicable to “emerging growth companies,” which could make our Class A common stock less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, and, for as long as we continue to be an “emerging growth company,” we intend to take advantage of certain exemptions from various reporting requirements applicable to other public companies but not to “emerging growth companies,” including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an “emerging growth company” for up to five years, or until the earliest of (i) the last day of the first fiscal year in which our annual gross revenues exceed $1 billion, (ii) the date that we become a “large accelerated filer” as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our Class A common stock that is held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter, or (iii) the date on which we have issued more than $1 billion in non-convertible debt during the preceding three year period. We cannot predict if investors will find our Class A common stock less attractive if we choose to rely on these exemptions. If some investors find our Class A common stock less attractive as a result of any choices to reduce future disclosure, there may be a less active trading market for our Class A common stock and our stock price may be more volatile.

We will incur significantly increased costs and devote substantial management time as a result of operating as a public company particularly after we are no longer an “emerging growth company.”

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. For example, we are required to comply with certain of the requirements of the Sarbanes-Oxley Act and the Dodd-Frank Wall Street Reform and Consumer Protection Act, as well as rules and regulations subsequently implemented by the Securities and Exchange Commission, and NASDAQ, our stock exchange, including the establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. We expect that compliance with these requirements will increase our legal and financial compliance costs and will make some activities more time consuming and costly. In addition, our management and other personnel will need to divert attention from operational and other business matters to devote substantial time to these public company requirements. In particular, we expect to incur significant expenses and devote substantial management effort toward ensuring compliance with the requirements of Section 404 of the Sarbanes-Oxley Act. In that regard, we currently do not have an internal audit function.

However, for as long as we remain an “emerging growth company” as defined in the JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not “emerging growth companies” including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We intend to take advantage of these reporting exemptions until we are no longer an “emerging growth company.”

Under the JOBS Act, “emerging growth companies” can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not “emerging growth companies.”

After we are no longer an “emerging growth company,” we expect to incur additional management time and cost to comply with the more stringent reporting requirements applicable to companies that are deemed accelerated filers or

large accelerated filers, including complying with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act.

We cannot predict or estimate the amount of additional costs we may incur as a result of becoming a public company or the timing of such costs.

We are exempt from certain corporate governance requirements since we are a “controlled company” within the meaning of the NASDAQ rules, and as a result our stockholders will not have the protections afforded by these corporate governance requirements.

MacAndrews controls more than 50% of our combined voting power. As a result, we are considered a “controlled company” for the purposes of NASDAQ rules and corporate governance standards, and therefore are permitted to, elect not to comply with certain NASDAQ corporate governance requirements, including those that would otherwise require our Board of Directors to have a majority of independent directors and require that we either establish compensation and nominating and corporate governance committees,

each comprised entirely of independent directors, or otherwise ensure that the compensation of our executive officers and nominees for directors are determined or recommended to the Board of Directors by the independent members of the Board of Directors. Accordingly, holders of our Class A common stock do not have the same protections afforded to stockholders of companies that are subject to all of the NASDAQ rules and corporate governance standards, and the ability of our independent directors to influence our business policies and affairs may be reduced.

Provisions in our charter and bylaws and provisions of Delaware law may delay or prevent our acquisition by a third party, which might diminish the value of our common stock.

Our amended and restated certificate of incorporation and amended and restated bylaws contain several provisions that may make it more difficult or expensive for a third party to acquire control of us without the approval of the Board of Directors. These provisions also may delay, prevent or deter a merger, acquisition, tender offer, proxy contest or other transaction that might otherwise result in our stockholders receiving a premium over the market price for their common stock. The provisions include, among others:

- a prohibition on actions by written consent of the stockholders;
- authorized but unissued shares of common stock and preferred stock that will be available for future issuance;
- the ability of our Board of Directors to increase the size of the Board of Directors and fill vacancies without a stockholder vote;
- provisions that have the same effect as a modified version of Section 203 of the Delaware General Corporation Law, an antitakeover law (as further described below); and
- advance notice requirements for stockholder proposals and director nominations.

Section 203 of the Delaware General Corporation Law may affect the ability of an “interested stockholder” to engage in certain business combinations, including mergers, consolidations or acquisitions of additional shares, for a period of three years following the time that the stockholder becomes an “interested stockholder.” An “interested stockholder” is defined to include persons owning directly or indirectly 15% or more of the outstanding voting stock of a corporation. We have elected in our amended and restated certificate of incorporation not to be subject to Section 203 of the Delaware General Corporation Law. Nevertheless, the amended and restated certificate of incorporation will contain provisions that have the same effect as Section 203 of the Delaware General Corporation Law, except that they provide that MacAndrews and its various successors and affiliates (and transferees of any of them) will not be deemed to be “interested stockholders,” regardless of the percentage of our stock owned by them, and accordingly will not be subject to such restrictions.

The provisions of our amended and restated certificate of incorporation and amended and restated bylaws, the significant common stock ownership of MacAndrews and the ability of the Board of Directors to create and issue a new series of preferred stock or implement a stockholder rights plan could discourage potential takeover attempts and reduce the price that investors might be willing to pay for shares of our common stock in the future, which could reduce the market price of our common stock.

We will be required to pay M&F TTP Holdings Two LLC (“M&F”) for certain tax benefits we may claim. In certain circumstances, payments under the Tax Receivable Agreement may be accelerated and/or significantly exceed the actual tax benefits we realize.

The only asset of the Company is its interest in vTv LLC. Class B common stock, together with the corresponding number of vTv Units, may be exchanged for shares of our Class A common stock, or for cash, at our option (as the managing member of vTv LLC). These exchanges of Class B common stock, together with the corresponding number of vTv LLC Units, may result in increases in the tax basis of the assets of vTv LLC that otherwise would not have been available. Such increases in tax basis are likely to increase (for tax purposes) depreciation and amortization deductions and therefore reduce the amount of income tax we would otherwise be required to pay in the future and may also decrease gain (or increase loss) on future dispositions of certain assets to the extent the increased tax basis is allocated to those assets. The IRS may challenge all or part of these tax basis increases and a court could sustain such

a challenge.

We have entered into a Tax Receivable Agreement with vTv Therapeutics Holdings (an entity which was dissolved in October 2015, but to which M&F became a successor) that will provide for the payment by us to M&F (or certain of its transferees or other assignees) of 85% of the amount of cash savings, if any, in U.S. federal, state and local income tax or franchise tax that we actually realize (or, in some circumstances, we are deemed to realize) as a result of (a) the exchange of Class B common stock, together with the corresponding number of vTv Units, for shares of our Class A common stock (or for cash), (b) tax benefits related to imputed interest deemed to be paid by us as a result of the Tax Receivable Agreement and (c) certain tax benefits attributable to payments under the Tax Receivable Agreement. Although the actual increase in tax basis and the amount and timing of any payments under the Tax Receivable Agreement will vary depending upon a number of factors, including the timing of exchanges, the price of shares of our Class A common stock at the time of the exchange, the nature of the assets, the extent to which such exchanges are taxable, the tax

rates then applicable, and the amount and timing of our income, we expect that the payments that we may make to M&F could be substantial.

M&F generally will not reimburse us for any payments that may previously have been made under the Tax Receivable Agreement even if the IRS subsequently disallows the tax basis increase or any other relevant tax item. Instead, any excess cash payments made by us to M&F will be netted against any future cash payments that we might otherwise be required to make under the terms of the Tax Receivable Agreement. However, we might not determine that we have effectively made an excess cash payment to M&F for a number of years following the initial time of such payment. As a result, in certain circumstances we could make payments to M&F under the Tax Receivable Agreement in excess of our cash tax savings. Our ability to achieve benefits from any tax basis increase and the payments to be made under the Tax Receivable Agreement, will depend upon a number of factors, including the timing and amount of our future income and the nature of our assets.

To the extent that we are unable to make payments under the Tax Receivable Agreement for any reason, such payments will be deferred and will accrue interest until paid. In addition, the Tax Receivable Agreement provides that, upon a merger, asset sale or other form of business combination or certain other changes of control or if, at any time, we elect an early termination of the Tax Receivable Agreement, our (or our successor's) obligations under the Tax Receivable Agreement with respect to exchanged or acquired Class B common stock, together with the corresponding number of vTv Units (whether exchanged or acquired before or after such change of control or early termination), would be required to be paid significantly in advance of the actual realization, if any, of any future tax benefits and would be based on certain assumptions, including that we would have sufficient taxable income to fully utilize the deductions arising from the increased tax deductions and tax basis and other benefits related to entering into the Tax Receivable Agreement, and, in the case of certain early termination elections, that any Class B common stock, together with the corresponding number of vTv Units, that have not been exchanged will be deemed exchanged for the market value of the Class A common stock at the time of termination. Consequently, it is possible that the actual cash tax savings realized by us may be significantly less than the corresponding Tax Receivable Agreement payments.

The only asset of the Company is its interest in vTv LLC, and accordingly it will depend on distributions from vTv LLC to pay taxes and expenses, including payments under the Tax Receivable Agreement. vTv LLC's ability to make such distributions may be subject to various limitations and restrictions.

The Company is a holding company, has no material assets other than its ownership of vTv Units and has no independent means of generating revenue or cash flow. vTv LLC is treated as a partnership for U.S. federal income tax purposes and, as such, is not subject to any entity-level U.S. federal income tax. Instead, taxable income will be allocated to holders of its common units, including us. As a result, we will incur U.S. federal, state and local income taxes on our allocable share of any net taxable income of vTv LLC. Under the terms of vTv LLC's Amended and Restated LLC Agreement, vTv LLC will be obligated to make tax distributions to holders of its common units, including us. In addition to tax expenses, we will also incur expenses related to our operations, including expenses under the Tax Receivable Agreement, which could be significant. We intend, as its managing member, to cause vTv LLC to make distributions in an amount sufficient to allow us to pay our taxes and operating expenses, including any payments due under the Tax Receivable Agreement. However, vTv LLC's ability to make such distributions may be subject to various limitations and restrictions including, but not limited to, restrictions on distributions that would either violate any contract or agreement to which vTv LLC is then a party, including potential debt agreements, or any applicable law, or that would have the effect of rendering vTv LLC insolvent. If vTv LLC does not distribute sufficient funds for us to pay our taxes or other liabilities, we may have to borrow funds, which could adversely affect our liquidity and subject us to various restrictions imposed by any such lenders. To the extent that we are unable to make payments under the Tax Receivable Agreement for any reason, such payments will be deferred and will accrue interest until paid.

Our organizational structure confers certain benefits upon M&F and certain of its successors and assigns that will not benefit Class A common stockholders to the same extent as it will benefit M&F.

Our organizational structure, including the fact that M&F owns more than 50% of the voting power of our outstanding voting stock and owns part of its economic interest in our business through vTv LLC, confers certain benefits upon M&F that will not benefit the holders of our Class A common stock to the same extent as it will benefit M&F. For example, the Tax Receivable Agreement will provide for the payment by us to M&F (or certain of its transferees or other assignees) of 85% of the amount of cash savings, if any, in U.S. federal, state and local income tax or franchise tax that we actually realize (or, in some circumstances, we are deemed to realize) as a result of (a) the exchange of Class B common stock, together with the corresponding number of vTv Units, for shares of our Class A common stock (or for cash), (b) tax benefits related to imputed interest deemed to be paid by us as a result of the Tax Receivable Agreement and (c) certain tax benefits attributable to payments under the Tax Receivable Agreement. Although we will retain 15% of the amount of such tax benefits, it is possible that the interests of M&F may in some circumstances conflict with our interests and the interests of our other stockholders. For example, M&F may have different tax positions from us, especially in light of the Tax Receivable Agreement, that could influence their decisions regarding whether and when we should dispose of assets, whether and when we should incur new or refinance existing indebtedness, and whether and when we should terminate the Tax Receivable Agreement and accelerate our obligations thereunder. In addition, the determination of future tax reporting positions, the structuring of

future transactions and the handling of any future challenges by any taxing authority to our tax reporting positions may take into consideration M&F's tax or other considerations, which may differ from the considerations of us or our other stockholders. To the extent that M&F is dissolved or liquidated, MacAndrews and/or its affiliates will succeed to the rights and obligations of M&F under the Tax Receivable Agreement, and the same considerations described above apply to any such successor parties.

ITEM 1B. UNRESOLVED STAFF COMMENTS
None.

ITEM 2. PROPERTIES
Our corporate headquarters and lab facilities are located in High Point, North Carolina, where we lease 43,040 square feet of mixed laboratory and office space in the Mendenhall Oaks office park. The lease agreement for this space continues through June 2018, with an option for early termination in June 2016.

We believe that our existing facilities are adequate for our current and expected future needs. We may seek to negotiate new leases or look for additional or alternate space for our operations. We believe that appropriate alternative space is readily available at similar rents.

ITEM 3. LEGAL PROCEEDINGS
We are not currently a party to any material legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES
None.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES
Market Information

Our Class A common stock began trading on the NASDAQ Global Select Market on July 30, 2015 under the symbol "VTVT". Prior to such time, there was no public market for our Class A common stock. The following table sets forth the high and low sale prices per share for our Class A common stock, as reported on the NASDAQ Global Select Market for the periods indicated since our IPO:

	High	Low
Calendar Quarter – 2015		
Third Quarter (commencing July 30, 2015)	$14.00	$5.27
Fourth Quarter	8.22	5.72

Dividend Policy

No cash dividends have ever been declared or paid on the common equity to date by the Company, and we do not currently plan to pay cash dividends in the foreseeable future.

Holders

As of March 4, 2016, there were approximately 15 holders of record of our Class A common stock and 30 holders of record of our Class B common stock. Because almost all of the shares of our Class A common stock are held by brokers, nominees and other institutions on behalf of shareholders, we are unable to estimate the total number of shareholders represented by these record holders.

Securities Authorized for Issuance under Equity Compensation Plans

The following table summarizes information about our equity compensation plans as of December 31, 2015. All outstanding option awards relate to our Class A common stock:

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights (a)	Weighted-average Exercise Price of Outstanding Options, Warrants and Rights (b)	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders			
2015 Omnibus Equity Incentive Plan	971,934	$ 11.31	2,278,066
Equity compensation plans not approved by security holders			
Total	971,934		2,278,066

During the year ended December 31, 2015, a total of 973,974 options to purchase our Class A common stock were granted to certain of our employees, directors and consultants under the 2015 Omnibus Equity Incentive Plan. These options vest and become exercisable ratably on a monthly basis generally over the first three years following the date of grant.

Performance Graph

The following graph shows a comparison from July 30, 2015 (the date our Class A common stock commenced trading on The NASDAQ Global Market) through December 31, 2015 of the cumulative total return for our Class A common stock, the NASDAQ Biotechnology Index and the NASDAQ Composite Index. The graph assumes an initial investment of $100 on July 30, 2015. The comparisons in the graph are not intended to forecast or be indicative of possible future performance of our common stock.

Issuer Purchases of Equity Securities

There have been no repurchases of the Company’s common stock during the fourth fiscal quarter of fiscal 2015.

ITEM 6. SELECTED FINANCIAL DATA

The following selected financial data should be read together with the information under “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and the notes to those financial statement included elsewhere in this Annual Report on Form 10-K. The selected statements of operations data for the years ended December 31, 2015, 2014 and 2013 and balance sheet data as of December 31, 2015 and 2014 set forth below have been derived from our audited financial statements included elsewhere in this Annual Report on Form 10-K. The selected balance sheet data as of December 31, 2013 set forth below has been derived from the audited financial statements for such year not included in this Annual Report on Form 10-K. The historical periods presented here are not necessarily indicative of future results.

	Year Ended December 31,		
(dollars in thousands, except for per share data)	2015	2014	2013
Statement of operations data:			