

**SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

**Amendment No. 1**  
to  
**FORM S-1**  
**REGISTRATION STATEMENT**  
*UNDER*  
**THE SECURITIES ACT OF 1933**

**ZAFGEN, INC.**

(Exact name of Registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**2834**  
(Primary Standard Industrial  
Classification Code Number)

**20-3857670**  
(I.R.S. Employer  
Identification No.)

**One Broadway, 8th Floor**  
**Cambridge, Massachusetts 02142**  
**(617) 401-3041**

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

**Thomas E. Hughes, Ph.D.**  
**President and Chief Executive Officer**  
**Zafgen, Inc.**  
**One Broadway, 8th Floor**  
**Cambridge, Massachusetts 02142**  
**(617) 401-3041**

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**Approximate date of commencement of proposed sale to public:** As soon as practicable after this Registration Statement becomes effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering:

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering:

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering:

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.

Large Accelerated Filer  Accelerated Filer   
Non-Accelerated Filer  (Do not check if a smaller reporting company) Smaller Reporting Company

**CALCULATION OF REGISTRATION FEE**

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price <sup>(1)</sup>	Amount of Registration Fee <sup>(2)(3)</sup>
Common Stock, par value \$0.001 per share	\$86,250,000	\$11,109

- (1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act. Includes the offering price of shares that the underwriters have the option to purchase to cover over-allotments, if any.
- (2) Calculated pursuant to Rule 457(o) under the Securities Act based on an estimate of the proposed maximum aggregate offering price.

(3) Previously paid.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

PRELIMINARY PROSPECTUS (Subject to Completion, dated April 28, 2014)

## Shares



### COMMON STOCK

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This is the initial public offering of shares of common stock of Zafgen, Inc. We are selling \_\_\_\_\_ shares of common stock.

Prior to this offering, there has been no public market for our common stock. The initial public offering price is expected to be between \$ \_\_\_\_\_ and \$ \_\_\_\_\_ per share.

We have applied to list our common stock on The NASDAQ Global Market under the symbol "ZFGN."

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012, and, as such, we have elected to take advantage of certain reduced reporting requirements for this prospectus and may elect to comply with certain reduced public company reporting requirements for future filings.

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	Per Share	Total
Initial public offering price	\$ _____	\$ _____
Underwriting discounts and commissions <sup>(1)</sup>	\$ _____	\$ _____
Proceeds to Zafgen, Inc. before expenses	\$ _____	\$ _____

(1) See "Underwriting" beginning on page 144 for additional information regarding underwriting compensation.

We have granted the underwriters an option to purchase up to \_\_\_\_\_ additional shares of common stock to cover over-allotments.

**Investing in our common stock involves a high degree of risk. See "[Risk Factors](#)" beginning on page 12.**

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to purchasers on or about \_\_\_\_\_, 2014.

**Leerink Partners**

**Canaccord Genuity**

**Cowen and Company**

**JMP Securities**

\_\_\_\_\_, 2014

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We and the underwriters have not authorized anyone to provide any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

**Until \_\_\_\_\_, 2014, all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.**

For investors outside of the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

## PROSPECTUS SUMMARY

*This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our consolidated financial statements and the related notes included elsewhere in this prospectus. You should also consider, among other things, the matters described under “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” in each case appearing elsewhere in this prospectus. Unless otherwise stated, all references to “us,” “our,” “ZFGN,” “we,” the “Company” and similar designations refer to Zafgen, Inc. and its subsidiaries.*

### Overview

We are a biopharmaceutical company dedicated to significantly improving the health and well-being of patients affected by obesity. Beloranib, our lead product candidate, is a novel, first-in-class, twice-weekly subcutaneous injection being developed for the treatment of multiple indications, including obesity and hyperphagia, or insatiable life-threatening hunger and hunger-related behaviors, in Prader-Willi Syndrome, or PWS, craniopharyngioma-associated obesity, and severe obesity in the general population.

### ***Beloranib for the Treatment of Obesity and Hyperphagia in PWS***

PWS is a rare and complex genetic disorder characterized by physiologic, cognitive and behavioral symptoms, including hyperphagia and obesity. We recently completed two Phase 2a clinical trials evaluating beloranib’s ability to reduce body weight and to improve hyperphagia, one in PWS patients and one in severely obese patients. In our Phase 2a clinical trials, we observed reductions in body weight, body mass and body fat content in both patient populations and reductions in hyperphagia-related behaviors in PWS patients. In January 2013, the U.S. Food and Drug Administration, or FDA, granted orphan designation for our application to treat PWS with beloranib. We plan to initiate a Phase 3 clinical program, consisting of two Phase 3 clinical trials, of beloranib in PWS patients in 2014 after finalizing the program design based on conversations with the FDA and certain European regulatory authorities. We filed an application to obtain orphan drug designation for beloranib as a treatment for PWS in the European Union in early 2014. We believe that rare conditions such as PWS afford us an opportunity to rapidly develop and commercialize beloranib using smaller, more focused and less costly clinical trials, relative to those required to develop beloranib for the broader severe obesity population.

PWS is characterized by hyperphagia resulting at least in part from impaired functioning of the hypothalamus, an area of the brain responsible for many functions including the desire to eat. Hyperphagia impairs the PWS patients’ ability to live independently, requiring costly and constant supervision to prevent overeating. Without supervision, PWS patients are likely to die prematurely as a result of choking, stomach rupture or tissue necrosis, or from complications caused by morbid obesity, such as right heart failure and respiratory failure. Based on our evaluation of published survival data, the average life expectancy of PWS patients is approximately 32 years of age. While a small number of PWS patients are cared for in costly group homes, the majority of PWS patients are cared for in their homes, and their families undertake substantial effort to create physical barriers to eating. These efforts result in extremely stressful environments, as caregivers often place locks and alarms on cabinets and refrigerators that contain food to impede PWS patients’ efforts to obtain food at all times. We estimate the typical annual cost of treating a PWS patient is \$100,000 to \$200,000, excluding the often significant costs of drug therapies related to other medical and psychological conditions and the costs of any lost time from work experienced by their families due to responsibilities related to the care of a PWS patient.

Published population studies estimate that the prevalence of PWS in the United States and in the European Union ranges from 1 in 8,000 to 1 in 50,000. PWS is diagnosed at an early age, typically in the first year of life, and we believe that, due to the severity of the condition and its unique attributes, the vast majority of patients affected by PWS are diagnosed. Approximately 50% of PWS patients are 13 years of age or older. We believe

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that further information regarding the prevalence of PWS will become available through a patient registry that is currently being developed by the Foundation for Prader-Willi Research.

There are currently no effective pharmacological treatments for obesity and hyperphagia in PWS. Furthermore, bariatric surgery is contraindicated in PWS patients due to poor outcomes related to an increased risk of rupture of the reduced stomach in the setting of sleeve gastrectomy or gastric bypass procedures, or rupture of the restricted esophagus in the setting of gastric banding procedures with the consequence of life-threatening gastric perforation.

### ***Beloranib for the Treatment of Craniopharyngioma-Associated Obesity***

Craniopharyngioma is a rare form of benign brain tumor that occurs near the optic nerve, pituitary gland and hypothalamus. Approximately 30% to 50% of cases of craniopharyngioma are diagnosed in childhood and adolescence. Manifestations of craniopharyngioma include visual disturbances, headaches and impairment to the hypothalamus-pituitary axis affecting hormone secretion. Treatment of these tumors commonly involves radical surgical removal of the tumor mass by endoscopy or craniotomy, followed by radiation treatment, which results in disruption or removal of neighboring structures including the hypothalamus. Depending on the degree of damage to the hypothalamus caused by tumor removal and subsequent radiation, there may be greater variation in hyperphagia and obesity prevalence in craniopharyngioma patients than PWS patients. Post-treatment hypothalamic dysfunction results in hyperphagia in approximately 50% of these patients, resulting in obesity and a worsened quality of life.

We plan to seek orphan drug designation for the treatment of craniopharyngioma-associated obesity in the United States and the European Union, and anticipate initiating a Phase 2a clinical trial, ZAF-221, evaluating the impact of beloranib treatment on body weight, body composition and hyperphagia in patients with craniopharyngioma-associated obesity in the first half of 2014.

Published population studies estimate that the incidence of craniopharyngioma is 0.13 to 0.17 per 100,000 per year, or approximately 400 to 500 cases per year in the United States and 650 to 850 cases per year in the European Union. We believe patients with craniopharyngioma-associated obesity have a longer life expectancy than PWS patients, which contributes to an increased risk of developing obesity-related co-morbid conditions such as type 2 diabetes in such patients.

Currently, there are no pharmacological agents for the treatment of hyperphagia and resultant obesity seen in patients with craniopharyngioma-associated obesity, and bariatric surgery is not frequently employed in this patient population. We believe this is related to perceived risks of surgical interventions in this population including increased risk of post-surgical complications.

### ***Treatment of Severe Obesity in the General Population***

In 2013, we completed a 12-week Phase 2a clinical trial of beloranib administered twice weekly in obese patients. We observed placebo-adjusted weight loss, or weight loss observed beyond that seen in the control arm, of up to 10.3% after 12 weeks of treatment with beloranib. In addition, we observed reductions in levels of low density lipoprotein cholesterol, C-reactive protein and systolic blood pressure. Patients treated with beloranib also reported reduced hunger, as assessed using a visual analog scale, a widely used self-reported measure of hunger and related endpoints.

Our long-term intention is to pursue clinical development of beloranib or another methionine aminopeptidase 2, or MetAP2, inhibitor as a treatment for severely obese patients in the general population. We believe this patient population would benefit from MetAP2 inhibitor treatment through the reduction of body

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weight and through improvement of severity or symptoms of other co-morbid conditions. We believe that MetAP2 inhibitors have the potential to offer this patient population, most of which is not adequately responsive to available therapies, substantial health and quality of life benefits. We intend to initiate a Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population. We are also evaluating additional proprietary MetAP2 inhibitors beyond beloranib as potential development candidates that would provide increased patient convenience in the form of oral dosing, or an otherwise improved clinical profile. A decision on whether to subsequently advance beloranib into pivotal trials for severe obesity or to leverage the opportunity to advance another MetAP2 inhibitor into early development for severe obesity is anticipated to be made on the basis of results obtained from our planned Phase 3 clinical program of beloranib in PWS patients and discussions with regulatory authorities.

The most effective current treatment for severe obesity is bariatric surgery, including procedures such as the Roux-en-Y gastric bypass, adjustable gastric banding, sleeve gastrectomy and biliopancreatic diversion. Bariatric surgery produces dramatic and sustained weight loss, ranging on average from 20% to 35% one year post-procedure, and reduces overall mortality, but it can result in numerous complications and adverse events including thrombotic events, such as pulmonary embolism, infection, internal bleeding, pulmonary disease and gastrointestinal obstruction, which sometimes requires reoperation during the post-operative period. Longer-term side effects of bariatric surgery, such as poor nutrient absorption, strictures and hemias, have also been observed.

Bariatric surgery eligibility criteria generally identify surgical candidates as those patients with body mass indices, or BMIs, greater than 40 kg/m<sup>2</sup>, or those with BMIs over 35 kg/m<sup>2</sup> who also have a significant and uncontrolled co-morbid condition. Based on these criteria, it is estimated conservatively that there will be at least 16 million adults in the United States eligible for bariatric surgery by the time beloranib or another MetAP2 inhibitor could become available commercially. In addition to the BMI and co-morbidity eligibility criteria, patients need to satisfy a number of other criteria in order to have bariatric surgery: a severely obese patient must not have any known endocrine causes of obesity, a drug or alcohol problem, or an uncontrolled psychological condition, and must understand and appreciate the risks of the surgical intervention. According to the American Society for Metabolic & Bariatric Surgery and to HealthGrades, the average cost of bariatric surgery in the United States is approximately \$22,000-\$38,000. As a result of these limiting criteria and the financial commitments required, only a few hundred thousand patients undergo bariatric surgery each year even though over 16 million patients in the United States are eligible for the surgery based on BMI alone.

The pharmaceutical industry has undertaken several waves of activity to discover and develop new drugs for the treatment of obesity. Relative to bariatric surgery, pharmaceutical treatments have produced modest efficacy. In addition, existing pharmacotherapeutics for obesity often have undesirable adverse event profiles.

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***Our Product Pipeline***

The following table summarizes our product pipeline and development status of our product candidates for the treatment of indications we are currently pursuing:

<b>Indication</b>	<b>Product Candidate</b>	<b>Stage of Development</b>	<b>Development Status</b>
Obesity and hyperphagia in PWS patients	Beloranib	Phase 2a	<ul style="list-style-type: none"> <li>•Phase 2a clinical trial completed</li> <li>•Phase 2a clinical trial report expected to be ready in the second quarter of 2014</li> <li>•Phase 3 clinical program design being finalized and expected to begin in 2014, pending input from regulatory authorities</li> </ul>
Craniopharyngioma-associated obesity	Beloranib	Phase 2a	<ul style="list-style-type: none"> <li>•Phase 2a clinical trial expected to start in the first half of 2014</li> </ul>
Severe obesity in the general population	Beloranib	Phase 2a	<ul style="list-style-type: none"> <li>•Phase 2a clinical trial completed</li> <li>•Phase 2b clinical trial expected to begin in the second half of 2014</li> </ul>
	Second-generation MetAP2 inhibitors	Pre-clinical	<ul style="list-style-type: none"> <li>•Advancement into pivotal trials under consideration</li> <li>•Development candidates under consideration</li> </ul>
Nonalcoholic steatohepatitis, or NASH, nonalcoholic fatty liver disease, abdominal obesity and type 2 diabetes	ZGN-839	Pre-clinical	<ul style="list-style-type: none"> <li>•Pre-clinical studies ongoing</li> <li>•Investigational New Drug Application, or IND, filing anticipated by the first half of 2015</li> </ul>

***Company History***

Zafgen was founded in 2005 to explore novel approaches to obesity therapeutics, including agents known to inhibit MetAP2 that had been found to drive unprecedented weight loss and metabolic improvements in mice. After performing a wide range of experiments to validate the effects of MetAP2 inhibitors in validated animal models, we committed the full resources of the company to testing the efficacy and safety of MetAP2 inhibition in obese patients and to establishing the feasibility of MetAP2 inhibitors for eventual commercialization. We identified beloranib as a suitable in-licensing candidate, and, in parallel with preparing beloranib for use in otherwise healthy but obese patients, we conducted our own chemistry program to identify compounds with complementary characteristics. After completing studies to establish preliminary safety, mechanism of action, manufacturing feasibility and clinical proof of concept, we advanced beloranib as a clinical development candidate and explored its application in severely obese patient populations. Our early clinical experience highlighted several key aspects of beloranib's actions, including rapid and robust weight loss, changes in circulating hormones known to impact fat metabolism, clinically significant reductions in cardiovascular disease risk markers and a particularly striking impact on hunger.

***Beloranib Mechanism of Action***

Beloranib is a novel, first-in-class injectable small molecule therapy with a unique mechanism of action that reduces hunger while stimulating the use of stored fat as an energy source. Beloranib is the first anti-obesity agent with the potential to address two important abnormalities that are present in the obese patient—hunger that is inappropriate relative to the amount of energy stored as fat and dysregulation of fat metabolism, which causes more fat to be made and stored in an obese patient than in a lean person. Beloranib acts through potent inhibition of MetAP2, an enzyme that modulates the activity of key cellular processes that control metabolism. MetAP2



inhibitors work, at least in part, by directing MetAP2 binding to cellular stress mediators, thereby reducing the tone of signals that drive lipid synthesis by the liver and fat storage throughout the body. In this manner, MetAP2 inhibition serves the purpose of re-establishing balance to the ways the body packages and metabolizes fat and glucose. MetAP2 inhibitors reduce the production of new fatty acid molecules by the liver and help convert stored fats into useful energy while reducing hunger.

We have completed five clinical trials, including two Phase 2a clinical trials, evaluating beloranib in over 200 patients. Although these clinical trials were of short duration and designed to demonstrate safety and tolerability, significant decreases in both body weight and sense of hunger were observed in patients treated with beloranib when compared to the placebo group. Additional clinical trials of longer-term treatment with beloranib designed to demonstrate efficacy are required before we can submit a New Drug Application for beloranib as a treatment for any indication that we are pursuing. In our planned Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population and our planned Phase 3 clinical program of beloranib as a treatment for PWS patients, patients will be treated with beloranib for a substantially longer period of time than as treated in our earlier clinical trials. In addition, we observed improvements in cardiovascular disease risk factors such as plasma total cholesterol, low density lipoprotein cholesterol and C-reactive protein. Across our completed clinical trials, beloranib has been well-tolerated at doses in the range of 1.0 mg to 2.0 mg administered twice weekly, and has not been associated with serious side effects. Laboratory safety measures, vital signs and electrocardiograms have been unremarkable in all completed clinical trials for all doses of beloranib tested.

### **Our Strategy**

Our objective is to be a leader in the discovery, development and commercialization of novel therapies to significantly improve the health and well-being of patients affected by obesity. Key elements of our strategy include:

- ***Advance the clinical development of beloranib in subpopulations of obese patients, including those with rare conditions, where obesity is a co-morbidity of an underlying condition.*** Diseases in this category include PWS, hypothalamic damage that is caused by trauma, surgical removal of tumors (including craniopharyngioma), radiation therapy of mid-brain tumors and monogenic loss of function mutations, including leptin deficiency and melanocortin receptor subclass 4 mutations. We believe that rare conditions such as PWS afford us an opportunity to rapidly develop and commercialize beloranib using smaller, more focused and less costly clinical trials, relative to those required to develop beloranib for the broader severe obesity population. Beloranib exerts its weight loss effects using a novel mechanism that does not appear to require fully functioning hypothalamic control pathways. We believe this mechanism is well-suited for patients with obesity that is caused by the failure of hypothalamic food intake control mechanisms, in particular the control of relentless and pathological hunger, or hyperphagia.
- ***Advance the clinical development of MetAP2 inhibitors for the treatment of severely obese patients in the general population, including those who are candidates for bariatric surgery.*** We believe the severely obese patient population would benefit from MetAP2 inhibitor treatment through the reduction of body weight and through improvement of other co-morbid conditions. Bariatric surgery results in significant weight loss, but the financial expense and the potential for complications, adverse events and longer-term side effects limit its overall adoption, with only a few hundred thousand patients in the United States undergoing bariatric surgery each year. Existing pharmacotherapies result in less weight loss than surgical options, and these therapies not only have undesirable side effects, but also have risk of abuse.
- ***Leverage the knowledge of our experienced team of drug developers that have deep expertise in the field of obesity, the function of MetAP2 inhibitors and metabolic diseases.*** Our management team has deep expertise in obesity and related metabolic diseases, the function of MetAP2 inhibitors, the strengths and weaknesses of current treatments for obesity and the ability to recognize the potential of novel therapies for the treatment of obesity. Our team is complemented by highly experienced external consultants and collaborators in the areas of drug discovery, development and regulatory approval.

- **Maintain flexibility in commercializing and maximizing the value of our development programs.** While we intend to develop and commercialize beloranib for indications such as PWS and other rare conditions causing obesity, we may enter into strategic relationships with biotechnology or pharmaceutical companies to realize the full value of beloranib or our other earlier-stage development programs. For beloranib, we may enter into one or more strategic relationships to access broader geographic markets or additional indications. These relationships could focus on specific patient populations and their caregivers, on regional development or on distribution and sales of beloranib.
- **Development of other potential product candidates.** We have a second program focused on the delivery of MetAP2 inhibitors with targeted tissue distribution that shows early promise in animal models of abdominal obesity, fatty liver and type 2 diabetes. Our lead MetAP2 inhibitor in this class of molecules is called ZGN-839. We believe that compounds such as ZGN-839 will have utility in the treatment of type 2 diabetes in humans, and will further cause improvements in cardiovascular risk factors including low density lipoprotein cholesterol. We plan to advance multiple candidate drugs into early development to establish clinical proof of concept, safety and tolerability of these molecules as a way to leverage our internal know-how in metabolic diseases and the effects of MetAP2 inhibitors. These compounds, typified by ZGN-839, could provide additional short-term value to our company through focused development partnerships and collaborations.

#### **Risks Associated With Our Business**

Our business is subject to many risks and uncertainties of which you should be aware before you decide to invest in our common stock. These risks are discussed more fully under “Risk Factors” in this prospectus. Some of these risks include:

- We depend almost entirely on the success of one product candidate, beloranib, which is still in Phase 2 clinical development. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, beloranib.
- Positive results from early clinical trials of beloranib are not necessarily predictive of the results of later clinical trials of beloranib. If we cannot replicate the positive results from our earlier clinical trials of beloranib in our later clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize beloranib. It may further be necessary to validate different or additional instruments for measuring subjective endpoints, and to show that beloranib has clinically meaningful impact on those endpoints in order to obtain regulatory approval.
- Failures or delays in the commencement or completion of our planned clinical trials of beloranib could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.
- We rely, and expect that we will continue to rely, on third parties to conduct any future clinical trials for beloranib. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize beloranib and our business could be substantially harmed.
- The number of patients suffering from PWS and craniopharyngioma is small and has not been established with precision. If the actual number of patients with either of these conditions is smaller than we estimate or if any approval that we obtain is based on a narrower definition of these patient populations, our revenue and ability to achieve profitability will be adversely affected, possibly materially.
- If we are unable to adequately protect our proprietary technology or maintain issued patents which are sufficient to protect beloranib, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.
- We are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing beloranib or our other product candidates, if approved.

- Our future success depends on our ability to retain our President and Chief Executive Officer, and to attract, retain and motivate qualified personnel.

#### **Implications of Being an Emerging Growth Company**

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
- reduced disclosure about our executive compensation arrangements;
- no non-binding advisory votes on executive compensation or golden parachute arrangements; and
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than \$1 billion in nonconvertible debt during the previous three years; or (iv) the last day of the fiscal year in which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock. Also, we have irrevocably elected to “opt out” of the exemption for the delayed adoption of certain accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

#### **Corporate History and Information**

We were incorporated under the laws of the State of Delaware in November 2005. Our principal executive office is located at One Broadway, 8<sup>th</sup> Floor, Cambridge, Massachusetts, and our telephone number is (617) 401-3041. Our website address is [www.zafgen.com](http://www.zafgen.com). We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus.

We own various U.S. federal trademark registrations and applications and unregistered trademarks, including the following trademarks referred to in this prospectus: *ZAFGEN*<sup>®</sup> and our corporate logo. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the <sup>®</sup> and <sup>™</sup> symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

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<b>THE OFFERING</b>	
Common stock offered by us	shares
Common stock to be outstanding after this offering	shares
Over-allotment option	We have granted the underwriters an option to purchase a maximum of            additional shares of common stock from us. The underwriters can exercise this option at any time within 30 days from the date of this prospectus.
Use of Proceeds	We estimate that we will receive net proceeds from the sale of shares of our common stock in this offering of approximately \$       million, or \$       million if the underwriters fully exercise their option to purchase additional shares, assuming an initial public offering price of \$       per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to advance the clinical development of beloranib as a treatment for obesity and hyperphagia in PWS patients and craniopharyngioma-associated obesity, to advance the clinical development of beloranib as a treatment for severe obesity in the general population, to continue the development of ZGN-839 and to fund new and ongoing research and development activities, working capital and other general corporate purposes. See “Use of Proceeds” for additional information.
Risk Factors	You should read carefully “Risk Factors” beginning on page 12 and other information included in this prospectus for a discussion of factors that you should consider before deciding to invest in shares of our common stock.
Proposed NASDAQ Global Market symbol	ZFGN
The number of shares of common stock to be outstanding after this offering is based on 4,580,669 shares of common stock outstanding as of February 28, 2014 and excludes:	
<ul style="list-style-type: none"><li>• 9,503,975 shares of common stock issuable upon exercise of outstanding options as of February 28, 2014 at a weighted average exercise price of \$0.47 per share;</li><li>• 1,056,257 shares of common stock reserved for future issuance under our Amended and Restated 2006 Stock Option Plan, or 2006 Stock Option Plan, as of February 28, 2014; and</li><li>•            shares of our common stock reserved for future issuance under our 2014 Stock Option and Incentive Plan, or 2014 Stock Option Plan, which will become effective upon the completion of this offering.</li></ul>	
Except as otherwise indicated, all information in this prospectus assumes or gives effect to:	
<ul style="list-style-type: none"><li>• the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into an aggregate of 94,687,505 shares of our common stock upon the completion of this offering;</li></ul>	

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- no exercise of the outstanding options described above;
- no exercise by the underwriters of their option to purchase up to an additional                      shares of our common stock in this offering;
- our amended and restated certificate of incorporation and our amended and restated by-laws, both of which we will file immediately prior to the completion of this offering; and
- a        -for-        reverse stock split of our common stock to be effected prior to the completion of this offering.

**SUMMARY CONSOLIDATED FINANCIAL DATA**

You should read the following summary consolidated financial data together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the “Selected Consolidated Financial Data” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” sections of this prospectus. We have derived the consolidated statement of operations data for the years ended December 31, 2011, 2012 and 2013 and for the cumulative period from inception (November 22, 2005) through December 31, 2013 and the consolidated balance sheet data as of December 31, 2013 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of results that should be expected in the future.

	<u>Year Ended December 31,</u>			<b>Cumulative Period from Inception (November 22, 2005) to December 31, 2013</b>
	<u>2011</u>	<u>2012</u>	<u>2013</u>	
	(in thousands, except per share data)			
<b>Statement of Operations Data:</b>				
Revenue	\$ —	\$ —	\$ —	\$ —
Operating expenses:				
Research and development	11,403	11,544	9,561	54,290
General and administrative	1,751	2,247	4,219	14,309
Total operating expenses	<u>13,154</u>	<u>13,791</u>	<u>13,780</u>	<u>68,599</u>
Loss from operations	<u>(13,154)</u>	<u>(13,791)</u>	<u>(13,780)</u>	<u>(68,599)</u>
Other income (expense):				
Interest income	—	—	—	120
Interest expense	—	(97)	—	(106)
Foreign currency transaction gains (losses), net	(3)	8	(247)	(243)
Total other expense, net	<u>(3)</u>	<u>(89)</u>	<u>(247)</u>	<u>(229)</u>
Net loss	<u>(13,157)</u>	<u>(13,880)</u>	<u>(14,027)</u>	<u>(68,828)</u>
Accretion of redeemable convertible preferred stock to redemption value	<u>(53)</u>	<u>(67)</u>	<u>(213)</u>	<u>(554)</u>
Net loss attributable to common stockholders	<u><u>\$ (13,210)</u></u>	<u><u>\$ (13,947)</u></u>	<u><u>\$ (14,240)</u></u>	<u><u>\$ (69,382)</u></u>
Net loss per share attributable to common stockholders, basic and diluted <sup>(1)</sup>	<u><u>\$ (3.05)</u></u>	<u><u>\$ (3.13)</u></u>	<u><u>\$ (3.11)</u></u>	
Weighted average common shares outstanding, basic and diluted <sup>(1)</sup>	<u><u>4,327</u></u>	<u><u>4,457</u></u>	<u><u>4,578</u></u>	
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited) <sup>(2)</sup>			<u><u>\$ (0.17)</u></u>	
Pro forma weighted average common shares outstanding, basic and diluted (unaudited) <sup>(2)</sup>			<u><u>84,190</u></u>	

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	As of December 31, 2013		
	Actual	Pro Forma(3)	Pro Forma As Adjusted(4)
(in thousands)			
<b>Balance Sheet Data:</b>			
Cash and cash equivalents	\$ 35,517	\$ 35,517	\$
Working capital(5)	34,443	34,443	
Total assets	38,138	38,138	
Redeemable convertible preferred stock	103,797	—	
Total stockholders' equity (deficit)	(68,574)	35,223	

(1) See Note 9 to our consolidated financial statements for further details on the calculation of basic and diluted net loss per share attributable to common stockholders.

(2) See Note 9 to our consolidated financial statements for further details on the calculation of basic and diluted pro forma net loss per share attributable to common stockholders.

(3) Pro forma balance sheet data give effect to the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into an aggregate of 94,483,404 shares of our common stock upon the completion of this offering.

(4) Pro forma as adjusted balance sheet data give effect to the pro forma balance sheet data adjustments described in footnote (3) above as well as the sale by us of \_\_\_\_\_ shares of our common stock in this offering at an assumed initial public offering price of \$ \_\_\_\_\_ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A \$1.00 increase (decrease) in the assumed initial public offering price of \$ \_\_\_\_\_ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity by \$ \_\_\_\_\_ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of \_\_\_\_\_ shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity by \$ \_\_\_\_\_ million, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted data above is illustrative only and will be adjusted based on the actual initial public offering price and other terms of our initial public offering determined at pricing.

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

## RISK FACTORS

*Investing in our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all other information in this prospectus, including our consolidated financial statements and related notes, before investing in our common stock. Any of the risk factors we describe below could adversely affect our business, financial condition or results of operations. The market price of our common stock could decline if one or more of these risks or uncertainties actually occur, causing you to lose all or part of the money you paid to buy our common stock. Additional risks that we currently do not know about or that we currently believe to be immaterial may also impair our business. Certain statements below are forward-looking statements. See “Cautionary Note Regarding Forward-Looking Statements” in this prospectus.*

### **Risks Related to Product Development, Regulatory Approval and Commercialization**

***We depend almost entirely on the success of one product candidate, beloranib, which is still in Phase 2 clinical development. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, beloranib.***

We currently have only one product candidate, beloranib, in clinical development, and our business depends almost entirely on its successful clinical development, regulatory approval and commercialization. We currently have no drug products for sale and may never be able to develop marketable drug products. Beloranib, which is currently in Phase 2 clinical development as a treatment for obesity and hyperphagia in Prader-Willi Syndrome, or PWS, craniopharyngioma-associated obesity, and severe obesity in the general population, will require substantial additional clinical development, testing and regulatory approval before we are permitted to commence its commercialization. Our other product candidates, including ZGN-839, are still in pre-clinical development stages. The clinical trials of our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and, if approved, market any product candidate. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through pre-clinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years and may include post-marketing studies and surveillance, which will require the expenditure of substantial resources beyond the proceeds we raise in this offering. Of the large number of drugs in development in the United States, only a small percentage will successfully complete the U.S. Food and Drug Administration, or FDA, regulatory approval process and is commercialized. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development and clinical trials, we cannot assure you that beloranib or any other of our product candidates will be successfully developed or commercialized.

We are not permitted to market beloranib in the United States until we receive approval of a New Drug Application, or an NDA, from the FDA, or in any foreign countries until we receive the requisite approval from such countries. We recently completed two Phase 2a clinical trials evaluating beloranib’s ability to reduce body weight and to improve hyperphagia, one in patients with PWS and one in severely obese patients. We expect that the FDA will require us to conduct at least one pivotal trial in order to submit an NDA for beloranib as a treatment for PWS patients. However, meeting requirements of the FDA or certain European regulatory authorities may require that we conduct additional pivotal trials. We expect that the FDA will also require us to complete a Phase 2b clinical trial and at least two Phase 3 clinical trials to submit an NDA for beloranib as a treatment for severe obesity in the general population, and may require that we conduct a cardiovascular outcomes trial. Pursuant to the FDA’s February 2007 draft guidance to industry on the development of weight management drugs, in order to reasonably estimate the safety of a weight-management drug, Phase 3 clinical trials must randomize approximately 3,000 subjects to active doses of the product and 1,500 subjects to placebo for one year of treatment. We have not yet commenced any of these clinical trials. We plan to initiate a Phase 3 clinical program, consisting of two Phase 3 clinical trials, of beloranib in PWS patients in 2014 after finalizing the program design based on conversations with the FDA and certain European regulatory authorities. We intend to engage in such discussions to determine if our proposed Phase 3 clinical trial protocols would be sufficient to support an NDA submission to the FDA and a



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marketing authorization application, or MAA, to the European Medicines Agency, or EMA, seeking approval of beloranib for the treatment of PWS. To initiate a Phase 3 clinical program for beloranib in PWS patients, we will also need to complete certain pre-clinical animal studies and obtain sufficient supply of finished drug. We plan to initiate a Phase 2a clinical trial of beloranib as a treatment for craniopharyngioma-associated obesity in the first half of 2014. We intend to initiate a Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population in the second half of 2014. We are also evaluating additional proprietary methionine aminopeptidase 2, or MetAP2, inhibitors beyond beloranib as potential development candidates that would provide increased patient convenience in the form of oral dosing, or an otherwise improved clinical profile. A decision on whether to subsequently advance beloranib into pivotal trials for severe obesity or to leverage the opportunity to advance another MetAP2 inhibitor into early development for severe obesity is anticipated to be made on the basis of results obtained from our planned Phase 3 clinical program of beloranib in PWS patients and discussions with regulatory authorities. Accordingly, obtaining approval of an NDA is a complex, lengthy, expensive and uncertain process, and the FDA and certain European regulatory authorities may delay, limit or deny approval of beloranib for many reasons, including, among others:

- we may not be able to demonstrate that beloranib is safe and effective in treating obesity and hyperphagia in PWS patients, craniopharyngioma-associated obesity or severe obesity in the general population, to the satisfaction of the FDA and certain European regulatory authorities;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA and certain European regulatory authorities for marketing approval;
- the FDA and certain European regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA and certain European regulatory authorities may require that we conduct additional clinical trials;
- the FDA and certain European regulatory authorities may not approve the formulation, labeling or specifications of beloranib;
- the contract research organizations, or CROs, that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;
- the FDA and certain European regulatory authorities may find the data from pre-clinical studies and clinical trials insufficient to demonstrate that beloranib's clinical and other benefits outweigh its safety risks;
- the FDA and certain European regulatory authorities may disagree with our interpretation of data from our pre-clinical studies and clinical trials;
- the FDA and certain European regulatory authorities may not accept data generated at our clinical trial sites;
- if our NDA, if and when submitted, is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional pre-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the FDA may require development of a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval or post-approval;
- the FDA and certain European regulatory authorities may not approve the manufacturing processes or facilities of third-party manufacturers with which we contract; or
- the FDA and certain European regulatory authorities may change their approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully market beloranib. Moreover, because our business is almost entirely dependent upon this one product candidate, any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

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***Positive results from early clinical trials of beloranib are not necessarily predictive of the results of later clinical trials of beloranib. If we cannot replicate the positive results from our earlier clinical trials of beloranib in our later clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize beloranib. It may further be necessary to validate different or additional instruments for measuring subjective endpoints, and to show that beloranib has clinically meaningful impact on those endpoints in order to obtain regulatory approval.***

Positive results from our Phase 1 and Phase 2a clinical trials of beloranib may not necessarily be predictive of the results from required later clinical trials. Similarly, even if we are able to complete our planned Phase 2b or Phase 3 clinical trials of beloranib according to our current development timeline, the positive results from our Phase 1 and Phase 2a clinical trials of beloranib may not be replicated in our Phase 2b or Phase 3 clinical trial results. We believe that the design of our Phase 3 clinical program of beloranib as a treatment for obesity and hyperphagia in PWS patients will differ in several respects from our recently completed Phase 2a clinical trial for PWS. For example, PWS patients will not only be living in closely-controlled PWS-specific group homes but also will be living in family homes. In addition, PWS patients will be treated with beloranib for greater than four weeks. In later-stage clinical trials, we will likely be subject to more rigorous statistical analyses. For example, the results of our Phase 2a clinical trial for severe obesity were based on a per protocol analysis of patients who completed the 12-week dosing in the clinical trial. We expect later-stage clinical trials to be evaluated based on an intent-to-treat analysis that includes all patients enrolled in the clinical trial, which may lead to different results. In addition, if we fail to validate a caregiver-administered PWS-specific hyperphagia-related behaviors questionnaire, or PWS-HQ, in time for it to be an effective tool to evaluate data from our Phase 3 clinical trial, our Phase 3 clinical program and, in turn, our regulatory filing may be delayed until we validate the tool or develop a new one. This can be a lengthy process. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, pre-clinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including previously unreported adverse events. Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in pre-clinical studies and clinical trials nonetheless failed to obtain FDA approval. If we fail to produce positive results in our planned Phase 2b or Phase 3 clinical trials of beloranib, the development timeline and regulatory approval and commercialization prospects for our leading product candidate, and, correspondingly, our business and financial prospects, would be materially adversely affected.

***Failures or delays in the commencement or completion of our planned clinical trials of beloranib could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.***

We plan to commence a Phase 3 clinical program of beloranib as a treatment for obesity and hyperphagia in PWS patients, a Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population and a Phase 2a clinical trial of beloranib as a treatment for craniopharyngioma-associated obesity. Successful completion of such clinical trials is a prerequisite to submitting an NDA to the FDA and, consequently, the ultimate approval and commercial marketing of beloranib. We do not know whether any of these Phase 2a, Phase 2b or Phase 3 clinical trials will begin or be completed on schedule, if at all, as the commencement and completion of clinical trials can be delayed or prevented for a number of reasons, including, among others:

- the FDA may deny permission to proceed with our planned Phase 2a, Phase 2b or Phase 3 clinical trials or any other clinical trials we may initiate, or may place a clinical trial on hold;
- delays in filing or receiving approvals or additional INDs that may be required;
- negative results from our ongoing pre-clinical studies;
- delays in reaching or failing to reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- inadequate quantity or quality of a product candidate or other materials necessary to conduct clinical trials, for example delays in the manufacturing of sufficient supply of finished drug product;

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- difficulties obtaining Institutional Review Board, or IRB, approval to conduct a clinical trial at a prospective site or sites;
- challenges in recruiting and enrolling patients to participate in clinical trials, including the size and nature of the patient population, the proximity of patients to trial sites, eligibility criteria for the clinical trial, the nature of the clinical trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications;
- severe or unexpected drug-related side effects experienced by patients in a clinical trial, including side effects previously identified in our completed clinical trials;
- delays in validating any self-reported measures of hunger and related endpoints utilized in a clinical trial;
- the FDA may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- reports from pre-clinical or clinical testing of other weight loss therapies that raise safety or efficacy concerns; and
- difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to rigors of the clinical trials, lack of efficacy, side effects, personal issues or loss of interest.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRBs, at the sites where the IRBs are overseeing a clinical trial, a data and safety monitoring board, or DSMB, overseeing the clinical trial at issue or other regulatory authorities due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a clinical hold;
- unforeseen safety issues, including any that could be identified in our ongoing pre-clinical carcinogenicity studies, adverse side effects or lack of effectiveness;
- changes in government regulations or administrative actions;
- problems with clinical supply materials; and
- lack of adequate funding to continue the clinical trial.

***Changes in regulatory requirements, FDA guidance or guidance from certain European regulatory authorities or unanticipated events during our clinical trials of beloranib may occur, which may result in changes to clinical trial protocols or additional clinical trial requirements, which could result in increased costs to us and could delay our development timeline.***

Changes in regulatory requirements, FDA guidance or guidance from certain European regulatory authorities or unanticipated events during our clinical trials may force us to amend clinical trial protocols or the FDA or certain European regulatory authorities may impose additional clinical trial requirements or change their positions on the acceptability of our trial designs or the clinical endpoints selected. For instance, the FDA issued draft guidance on developing products for weight management in February 2007, but this guidance may be revised in the near future. In March 2012, the FDA's Endocrinologic and Metabolic Drugs Advisory Committee met to discuss possible changes to how the FDA evaluates the cardiovascular safety of weight-management drugs. Amendments to our clinical trial protocols would require resubmission to the FDA and IRBs for review and approval, which may adversely impact the cost, timing or successful completion of a clinical trial. In addition, we may be required to complete additional clinical trials, or the FDA and certain European regulatory authorities may impose stricter approval conditions. If we experience delays completing, or if we terminate, any of our clinical trials, or if we are required to conduct additional clinical trials, the commercial prospects for beloranib may be harmed and our ability to generate product revenue will be delayed.

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***We rely, and expect that we will continue to rely, on third parties to conduct any future clinical trials for beloranib. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize beloranib and our business could be substantially harmed.***

We enter into agreements with third-party CROs to provide monitors for and to manage data for our ongoing clinical trials. We rely heavily on these parties for execution of clinical trials for beloranib and control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these clinical trials and the management of data developed through the clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with current Good Clinical Practices, or cGCPs, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any products in clinical development. The FDA enforces these cGCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. In addition, our clinical trials must be conducted with product produced under current Good Manufacturing Practices, or cGMPs, regulations and will require a large number of test subjects. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties.

Although we do design our clinical trials for beloranib, CROs conduct all of the clinical trials. As a result, many important aspects of our drug development programs are outside of our direct control. In addition, the CROs may not perform all of their obligations under arrangements with us or in compliance with regulatory requirements, but we remain responsible and are subject to enforcement action that may include civil penalties up to and including criminal prosecution for any violations of FDA laws and regulations during the conduct of our clinical trials. If the CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development and commercialization of beloranib may be delayed or our development program materially and irreversibly harmed. We cannot control the amount and timing of resources these CROs devote to our program or beloranib. If we are unable to rely on clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of our clinical trials and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other

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reasons, any such clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize beloranib. As a result, our financial results and the commercial prospects for beloranib in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

***The number of patients suffering from PWS and craniopharyngioma is small and has not been established with precision. If the actual number of patients with either of these conditions is smaller than we estimate or if any approval that we obtain is based on a narrower definition of these patient populations, our revenue and ability to achieve profitability will be adversely affected, possibly materially.***

There is no current patient registry or other method of establishing with precision the actual number of patients with PWS or craniopharyngioma in any geography. Published population studies estimate that the prevalence of PWS in the United States and in the European Union ranges from 1 in 8,000 to 1 in 50,000. Published population studies estimate that the incidence of craniopharyngioma is 0.13 to 0.17 per 100,000 per year, or approximately 400 to 500 cases per year in the United States and 650 to 850 cases per year in the European Union. The total addressable market opportunity for beloranib for the treatment of patients with PWS or craniopharyngioma-associated obesity will ultimately depend upon, among other things, the diagnosis criteria included in the final label for beloranib, if approved for sale for these indications, acceptance by the medical community and patient access, product pricing and reimbursement. If the actual number of PWS or craniopharyngioma patients is lower than we believe or if any approval that we obtain is based on a narrower definition of these patient populations, then the potential markets for beloranib for these indications will be smaller than we anticipate.

In addition, we currently plan to seek approval of beloranib initially for the treatment adult patients with PWS and craniopharyngioma-associated obesity. We are currently engaged in discussions with the FDA regarding the age ranges for adult patients, adolescent patients, or pediatric patients. Approximately 50% of PWS patients are 13 years of age or older. To support approval for younger patients, we will need to conduct pediatric clinical trials of beloranib for the treatment of pediatric and adolescent patients with PWS or craniopharyngioma-associated obesity, but we do not yet have plans regarding when these trials will commence. As a result, any FDA approval would likely, at least initially, be limited to use for treating adult patients with PWS or craniopharyngioma-associated obesity. This would limit our initial product revenue and may make it more difficult for us to achieve or maintain profitability.

***We rely completely on third-party suppliers to manufacture our clinical drug supplies for beloranib, and we intend to rely on third parties to produce commercial supplies of beloranib and pre-clinical, clinical and commercial supplies of any future product candidate.***

We do not currently have, nor do we plan to acquire, the infrastructure or capability to internally manufacture our clinical drug supply of beloranib, or any future product candidates, for use in the conduct of our pre-clinical studies and clinical trials, and we lack the internal resources and the capability to manufacture any product candidates on a clinical or commercial scale. The facilities used by our contract manufacturers to manufacture the active pharmaceutical ingredient and final drug product must be approved by the FDA and other comparable foreign regulatory agencies pursuant to inspections that would be conducted after we submit our NDA or relevant foreign regulatory submission to the applicable regulatory agency.

We do not control the manufacturing process of, and are completely dependent on, our contract manufacturers to comply with cGMPs for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel. Furthermore, all of our contract manufacturers are engaged with other companies to supply

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and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our contract manufacturers' facilities generally. If the FDA or an applicable foreign regulatory agency does not approve these facilities for the manufacture of our product candidates or if it withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would adversely impact our ability to develop, obtain regulatory approval for or market our product candidates.

We are currently in the process of manufacturing finished drug product for use in our upcoming clinical trials. Sterile drug substance is currently in hand. Finished drug product, diluent and placebo are expected to be available in the third quarter of 2014. Aside from our planned Phase 2a clinical trial in patients with craniopharyngioma-associated obesity, we will not be able to commence any additional clinical trials without the production of additional finished drug product. The manufacturing process is under active development and these projections could change based on delays encountered with manufacturing activities, equipment scheduling and material lead times. Any such delays in the manufacturing of finished drug product could delay our planned clinical trials of beloranib, which could delay, prevent or limit our ability to generate revenue and continue our business.

We do not have long-term supply agreements in place with our contractors, and each batch of beloranib is individually contracted under a quality and supply agreement. If we engage new contractors, such contractors must be approved by the FDA and other applicable foreign regulatory agencies. We plan to continue to rely upon contract manufacturers and, potentially, collaboration partners to manufacture commercial quantities of beloranib, if approved. Our current scale of manufacturing is adequate to support all of our needs for clinical trial supplies and launch for orphan markets. For peak usage in orphan markets and for indications with larger populations of affected patients, we will need to identify contract manufacturers or partners to produce beloranib on a larger scale.

***If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell beloranib, we may not be able to generate any revenue.***

We do not currently have an infrastructure for the sales, marketing and distribution of pharmaceutical products. In order to market beloranib, if approved by the FDA or any other regulatory body, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition and prospects will be materially adversely affected.

***Even if we receive marketing approval for beloranib in the United States, we may never receive regulatory approval to market beloranib outside of the United States.***

We intend to pursue marketing approval of beloranib in the European Union and in other countries worldwide. In order to market any product outside of the United States, we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional product candidate testing and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in others. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such

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approval would impair our ability to market beloranib in such foreign markets. Any such impairment would reduce the size of our potential market, which could have a material adverse impact on our business, results of operations and prospects.

***Even if we receive marketing approval for beloranib, it may not achieve broad market acceptance, which would limit the revenue that we generate from its sales.***

The commercial success of beloranib, if approved by the FDA or EMA or other applicable regulatory authorities, will depend upon the awareness and acceptance of beloranib among the medical community, including physicians, patients and healthcare payors. Market acceptance of beloranib, if approved, will depend on a number of factors, including, among others:

- beloranib's demonstrated ability to treat obesity and hyperphagia in PWS patients, craniopharyngioma-associated obesity, or severe obesity in the general population and, if required by any applicable regulatory authority in connection with the approval for these indications, to provide patients with incremental health benefits, as compared with other available weight loss therapies, devices or surgeries;
- the relative convenience and ease of subcutaneous injections as the necessary method of administration of beloranib, including as compared with other treatments for severely obese patients;
- the prevalence and severity of any adverse side effects associated with beloranib, such as nausea, vomiting, headaches and difficulty sleeping or falling asleep;
- limitations or warnings contained in the labeling approved for beloranib by the FDA;
- availability of alternative treatments, including a number of competitive obesity therapies already approved or expected to be commercially launched in the near future;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of beloranib through marketing efforts;
- our ability to obtain sufficient third-party coverage or reimbursement; and
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage.

If beloranib is approved but does not achieve an adequate level of acceptance by patients, physicians and payors, we may not generate sufficient revenue from beloranib to become or remain profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that, in addition to treating obesity in patients, beloranib also provides incremental health benefits to patients. Our efforts to educate the medical community and third-party payors about the benefits of beloranib may require significant resources and may never be successful.

***Our product candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.***

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. In our recently completed Phase 2a clinical trials

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evaluating beloranib's ability to reduce body weight and to improve hyperphagia, the main adverse events, or AEs, including those leading to drop-outs, in patients dosed with beloranib, have been sleep disturbances, principally manifested as delayed onset of sleep, nausea and vomiting.

The safety data we have disclosed to date represents our interpretation of the data at the time of disclosure and it is subject to our further review and analysis. There have been no serious adverse events, or SAEs, attributed to beloranib in our clinical trials. However, SAEs that are not characterized by clinical investigators as possibly related to beloranib or SAEs that occur in small numbers may not be disclosed to the public until such time the various documents submitted to the FDA as part of the approval process are made public. We are unable to determine if the subsequent disclosure of SAEs will have an adverse effect on our stock price. In addition, our interpretation of the safety data from our clinical trials is contingent upon the review and ultimate approval of the FDA. The FDA may not agree with our methods of analysis or our interpretation of the results.

Further, if beloranib receives marketing approval and we or others identify undesirable side effects caused by the product (or any other similar product) after the approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as a "boxed" warning or a contraindication;
- we may be required to change the way the product is distributed or administered, conduct additional clinical trials or change the labeling of the product;
- we may decide to remove the products from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing our product candidates and significantly impact our ability to successfully commercialize our product candidates and generate revenues.

### ***Even if we receive marketing approval for beloranib, we may still face future development and regulatory difficulties.***

Even if we receive marketing approval for beloranib, regulatory authorities may still impose significant restrictions on beloranib's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. Beloranib will also be subject to ongoing FDA and EMA requirements governing the labeling, packaging, storage and promotion of the product and recordkeeping and submission of safety and other post-market information. The FDA has significant post-market authority, including, for example, the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate serious safety risks related to the use of a drug. The FDA also has the authority to require, as part of an NDA or post-approval, the submission of a REMS. Any REMS required by the FDA may lead to increased costs to assure compliance with new post-approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue.

Manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMPs and other regulations. If we or a regulatory agency discover problems with beloranib, such as adverse events of unanticipated severity or frequency, or problems with the facility where beloranib is manufactured, a regulatory agency may impose



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restrictions on beloranib, the manufacturer or us, including requiring withdrawal of beloranib from the market or suspension of manufacturing. If we, beloranib or the manufacturing facilities for beloranib fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw marketing approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or request that we initiate a product recall.

***Competing technologies could emerge, including devices and surgical procedures, adversely affecting our opportunity to generate revenue from the sale of beloranib.***

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in a number of jurisdictions, many of which have substantially greater name recognition, commercial infrastructures and financial, technical and personnel resources than we have. Established competitors may invest heavily to quickly discover and develop novel compounds that could make beloranib obsolete or uneconomical. Any new product that competes with an approved product may need to demonstrate compelling advantages in efficacy, convenience, tolerability and safety to be commercially successful. Other competitive factors, including generic competition, could force us to lower prices or could result in reduced sales. In addition, new products developed by others could emerge as competitors to beloranib. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

There are no current pharmacological treatments for regulating hunger and hyperphagia-related behaviors of PWS patients and craniopharyngioma patients, and bariatric surgery is contraindicated in PWS patients and not frequently employed in craniopharyngioma patients. We are aware of a clinical trial planned by Ferring Pharmaceuticals, Inc. to evaluate the use of oxytocin, a brain peptide hormone hypothesized to increase trust, reduce anxiety and improve behavior in patients with PWS. We also are aware of a clinical trial being planned by Essentialis, Inc. to evaluate the safety and tolerability of controlled-release diazoxide in PWS patients and to explore the effects of diazoxide on hyperphagia-related behaviors and energy expenditure. In addition, any of our competitors may develop a drug to treat PWS patients at any time. We are not aware of any clinical trials of drugs specifically targeting patients with craniopharyngioma-associated obesity, or in severe obesity in general.

Our potential competitors in the severe obesity market include bariatric surgery providers, and, in addition, other potential approaches which utilize various implantable devices or surgical tools are in development, by companies such as Allergan, Inc., Boston Scientific Corporation, Covidien Ltd., EnteroMedics, Inc., GI Dynamics, Inc., Johnson & Johnson and Medtronic, Inc. In addition, beloranib will compete with orlistat, phentermine/topiramate and lorcaserin, three recently approved and currently marketed pharmaceutical products in the United States for the treatment of obesity, and several older agents, indicated for short-term administration, including phentermine, phendimetrazine, benzphetamine and diethylpropion. Orlistat is marketed in the United States by Roche Group under the brand name Xenical and over-the-counter in the United States at half the prescribed dose by GlaxoSmithKline under the brand name alli. In June 2013, Arena Pharmaceuticals, Inc. launched its lorcaserin product, which is marketed in the United States under the name Belviq and in September 2012, Vivus, Inc. commercially launched its combination product, phentermine/topiramate, under the trade name Qsymia. Despite the large market opportunity for anti-obesity agents, there are relatively few competitive products in late-stage clinical development. In December 2013, Orexigen Therapeutics, Inc., which is developing

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Contrace, resubmitted its NDA based on a recently completed cardiovascular outcomes trial. Other companies pursuing pharmaceutical treatments for obesity include Neurosearch A/S, Novo Nordisk A/S and Takeda Pharmaceutical Company Limited.

***Our future growth depends, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.***

Our future profitability will depend, in part, on our ability to commercialize beloranib in foreign markets for which we intend to rely on collaboration with third parties. If we commercialize beloranib in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for beloranib in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of beloranib could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

***We are subject to healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of beloranib, if approved. Our future arrangements with third-party payors will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute beloranib, if we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- The federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid.
- The federal False Claims Act imposes criminal and civil penalties, including those from civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government.
- The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for

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executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

- The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.
- The federal transparency requirements, sometimes referred to as the “Sunshine Act,” under the Patient Protection and Affordable Care Act, require manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests.
- Analogous state laws and regulations, such as state anti-kickback and false claims laws and transparency laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and drug pricing.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could be costly. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales team, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines and exclusion from government funded healthcare programs, such as Medicare and Medicaid, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

***The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted off-label uses, we may become subject to significant liability.***

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as beloranib, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product’s approved labeling. If we receive marketing approval for beloranib as a treatment for obesity and hyperphagia in PWS patients or craniopharyngioma-associated obesity, physicians may nevertheless prescribe beloranib to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of beloranib, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

***Even if approved, reimbursement policies could limit our ability to sell beloranib.***

Market acceptance and sales of beloranib will depend on reimbursement policies and may be affected by healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels for those medications. Cost containment is a primary concern in the U.S. healthcare industry and elsewhere.

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Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that reimbursement will be available for beloranib and, if reimbursement is available, the level of such reimbursement. Reimbursement may impact the demand for, or the price of, beloranib. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize beloranib.

In some foreign countries, particularly in Canada and European countries, the pricing of prescription pharmaceuticals is subject to strict governmental control. In these countries, pricing negotiations with governmental authorities can take six to 12 months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of beloranib with other available therapies. If reimbursement for beloranib is unavailable in any country in which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical trials, or if pricing is set at unsatisfactory levels, our operating results could be materially adversely affected.

***Even though we have received orphan drug designation for PWS, we may not receive orphan drug exclusivity for beloranib.***

As part of our business strategy, we have obtained orphan drug designation in the United States for beloranib for the treatment of patients with PWS. In the United States, the company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for a period of seven years. This orphan drug exclusivity prevents the FDA from approving another application, including a full NDA to market the same drug for the same orphan indication, except in very limited circumstances, including when the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. For purposes of small molecule drugs, the FDA defines “same drug” as a drug that contains the same active chemical entity and is intended for the same use as the drug in question. To obtain orphan drug exclusivity for a drug that shares the same active chemical entity as an already orphan designated drug, it must be demonstrated to the FDA that the drug is safer or more effective than the approved orphan designated drug, or that it makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition or if another drug with the same active moiety is determined to be safer, more effective, or represents a major contribution to patient care.

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

In addition to the development of beloranib, we may pursue development of our other early-stage development programs. None of our other potential product candidates has commenced any clinical trials, and there are a number of FDA and certain European regulatory requirements that we must satisfy before we can commence clinical trials. Satisfaction of these requirements will entail substantial time, effort and financial resources. We may never satisfy these requirements. Any time, effort and financial resources we expend on our other early-stage development programs may adversely affect our ability to continue development and commercialization of beloranib, and we may never commence clinical trials of such development programs despite expending significant resources in pursuit of their development. If we do commence clinical trials of our other potential product candidates, such product candidates may never be approved by the FDA or the EMA.

## **Risks Relating to Our Intellectual Property Rights**

***If we are unable to adequately protect our proprietary technology or maintain issued patents which are sufficient to protect beloranib, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.***

Our commercial success will depend in part on our success in obtaining and maintaining issued patents and other intellectual property rights in the United States and elsewhere and protecting our proprietary technology. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability.

Our owned and licensed patents and patent applications relate to beloranib compositions of matter, formulations, polymorphs, methods of treating obesity using dosing regimens of beloranib, and methods of treating hypothalamic obesity. The issued U.S. and European patents generally directed to beloranib compositions of matter are exclusively licensed and will each expire in 2019. We own an issued U.S. patent relating to beloranib polymorph compositions of matter that will expire in 2031 and an issued U.S. patent to methods of treating obesity that will expire in 2029. We own pending patent applications in Europe to beloranib polymorph composition of matter and methods of treating obesity that we expect to expire, once issued, in 2031.

As of February 28, 2014, we own two issued U.S. patents, eight pending U.S. patent applications and foreign counterpart applications, and one Patent Cooperation Treaty, or PCT, application that will allow us to seek corresponding protection worldwide, all of which relate to beloranib. We have a license to two U.S. issued patents, one with corresponding issued foreign counterpart patents, that also relate to beloranib. We also co-own one patent application relating to methods of using beloranib with an option to exclusively license the co-owner rights.

As of February 28, 2014, we own seven pending U.S. patent applications with pending foreign counterpart applications and five PCT patent applications, all of which relate to our MetAP2 inhibitor program. Of these, one pending U.S. patent application with pending foreign counterpart patent applications and one PCT patent application relate to our early-stage product candidate ZGN-839.

As of February 28, 2014, we own two pending U.S. patent applications with pending foreign counterpart patent applications, one pending PCT patent application and two U.S. provisional patent applications that relate to our second-generation MetAP2 inhibitor program.

We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect beloranib or our other product candidates. Other parties have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Patents, if issued, may be challenged, deemed unenforceable, invalidated, or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, *ex parte* reexamination, or *inter partes* review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition, post-grant review, or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. Thus, any patents that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize beloranib.

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Furthermore, though an issued patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Competitors may also be able to design around our patents. Other parties may develop and obtain patent protection for more effective technologies, designs or methods. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, vendors, former employees and current employees. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales.

Our ability to enforce our patent rights depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product. Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time-consuming and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents covering beloranib are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered beloranib, our financial position and results of operations would also be materially and adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents, or any of our pending patent applications, if issued, will include claims having a scope sufficient to protect beloranib or any other products or product candidates;
- any of our pending patent applications will issue as patents;
- we will be able to successfully commercialize beloranib, if approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our patents and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe our patents;
- any of our patents will be found to ultimately be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- that our commercial activities or products will not infringe upon the patents of others.

We rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. We also have agreements with our employees and selected consultants that obligate them to assign their inventions to us and have non-compete agreements with some, but not all, of our consultants. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

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***We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing beloranib, if approved.***

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties.

The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that beloranib or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing another party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license. In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing beloranib.

Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, intellectual property litigation or claims could force us to do one or more of the following:

- cease developing, selling or otherwise commercializing beloranib;
- pay substantial damages for past use of the asserted intellectual property;
- obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and
- in the case of trademark claims, redesign, or rename, beloranib to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time-consuming.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

***We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.***

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

The U.S. Patent and Trademark Office, or U.S. PTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the

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patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

***We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.***

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

***Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.***

If we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent covering our product candidate, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the U.S. PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review and equivalent proceedings in foreign jurisdictions, e.g., opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would have a material adverse impact on our business.



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***We do not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.***

Filing, prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. 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.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***We are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing beloranib or our other product candidates, if approved.***

We have licensed our rights to beloranib from Chong Kun Dang Pharmaceutical Corp. of South Korea, or CKD. Our license with CKD imposes various obligations on us, including a requirement to use commercially reasonable efforts to develop beloranib and provides CKD the right to terminate the license thereunder in the event of a material breach. For example, CKD may allege that we have breached our license agreement and may accordingly seek to terminate our license with them. Termination of our license from CKD could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize beloranib, if approved, as well as harm our competitive business position and our business prospects. We also have an exclusive license with Children's Medical Center Corporation, or Children's, pursuant to which we exclusively licensed certain patient rights relating to decreasing the growth of fat tissue from Children's on a worldwide basis.

We may enter into additional license(s) to third-party intellectual property that are necessary or useful to our business. Future licensor(s) may also allege that we have breached our license agreement and may accordingly seek to terminate our license with them. In addition, future licensor(s) may decide to terminate our license at will. If successful, this could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize a product candidate or product, if approved, as well as harm our competitive business position and our business prospects.

***We have not yet registered trademarks for a commercial trade name for beloranib and failure to secure such registrations could adversely affect our business.***

We have not yet registered trademarks for a commercial trade name for beloranib. Any future trademark applications may be rejected during trademark registration proceedings. Although we would be given an

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opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the U.S. PTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we propose to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

***If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent terms and obtaining data exclusivity for beloranib, our business may be materially harmed.***

Depending upon the timing, duration and specifics of FDA marketing approval of beloranib, one or more of the U.S. patents we license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, 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, we may not be granted an extension because of, for example, 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. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected.

***Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.***

The United States has recently enacted and is currently implementing the America Invents Act of 2011, wide-ranging patent reform legislation. Further, 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. In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the U.S. PTO, 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 or future patents.

***We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers.***

Our employees have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we are not aware of any claims currently pending against us, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of the former employers of our employees. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying money claims, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize beloranib, which would materially adversely affect our commercial development efforts.

## **General Company-Related Risks**

***We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.***

As of February 28, 2014, we had ten full-time employees and two part-time employees, and in connection with becoming a public company, we expect to increase our number of employees and the scope of our operations. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of beloranib. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize beloranib, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

***Our future success depends on our ability to retain our President and Chief Executive Officer, and to attract, retain and motivate qualified personnel.***

We are highly dependent on Dr. Thomas E. Hughes, our President and Chief Executive Officer. We have entered into an employment agreement with Dr. Hughes, but he may terminate his employment with us at any time. Although we do not have any reason to believe that we will lose the services of Dr. Hughes in the foreseeable future, the loss of his services might impede the achievement of our research, development and commercialization objectives. We also do not have any key-man life insurance on Dr. Hughes. We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us and may not be subject to our standard non-compete agreements. Recruiting and retaining qualified scientific personnel and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

***Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and applicable non-U.S. regulators, provide accurate information to the FDA and applicable non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. 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 restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have

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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 be ineffective 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 fines or other sanctions.

### ***We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability.***

The use of beloranib in clinical trials and the sale of beloranib, if approved, exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others selling or otherwise coming into contact with beloranib. 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, including as a result of interactions with alcohol or other drugs, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of patients from our clinical trials;
- substantial monetary awards to patients or other claimants;
- decreased demand for beloranib or any future product candidates following marketing approval, if obtained;
- damage to our reputation and exposure to adverse publicity;
- increased FDA warnings on product labels;
- litigation costs;
- distraction of management's attention from our primary business;
- loss of revenue; and
- the inability to successfully commercialize beloranib or any future product candidates, if approved.

We maintain product liability insurance coverage for our clinical trials with a \$5.0 million annual aggregate coverage limit. Nevertheless, our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. 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, including if insurance coverage becomes increasingly expensive. If and when we obtain marketing approval for beloranib, we intend to expand our insurance coverage to include the sale of commercial products; however, we may not be able to obtain this product liability insurance on commercially reasonable terms. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our financial condition, business and prospects could be materially adversely affected.

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***We must maintain effective internal control over financial reporting, and if we are unable to do so, the accuracy and timeliness of our financial reporting may be adversely affected, which could have a material adverse effect on our business and stock price.***

We must maintain effective internal control over financial reporting in order to accurately and timely report our results of operations and financial condition. In addition, once we are a public company, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, will require, among other things, that we assess the effectiveness of our disclosure controls and procedures quarterly and the effectiveness of our internal control over financial reporting at the end of each fiscal year. We anticipate being first required to issue management's annual report on internal control over financial reporting, pursuant to Section 404 of the Sarbanes-Oxley Act, in connection with issuing our consolidated financial statements as of and for the year ending December 31, 2015.

During the course of preparing for this offering, we determined that material adjustments to various accounts were necessary, which required us to restate our consolidated financial statements as of and for the year ended December 31, 2011 and for the period from inception (November 22, 2005) through December 31, 2011 that had been previously audited by another independent audit firm. These adjustments leading to a restatement of those consolidated financial statements led us to conclude that we had material weaknesses in internal control over financial reporting as of December 31, 2011 as follows: (i) we did not maintain effective controls over accounting policies and application of GAAP—specifically, we did not maintain and communicate sufficient accounting policies, which limited our ability to make accounting decisions and to detect and correct accounting errors; and (ii) we did not maintain a sufficient complement of resources with an appropriate level of accounting knowledge, experience and training commensurate with our structure and financial reporting requirements.

During 2013, we executed on various remediation efforts, including ensuring we had sufficient resources with the appropriate technical accounting expertise and putting in place formalized policies and procedures to ensure complete and accurate consolidated financial statements are prepared. In that year, we hired additional senior accounting and finance employees, including a Chief Financial Officer with significant biotechnology industry experience, and engaged external consultants with significant financial and accounting technical experience. These additional resources have enabled us to (i) implement standardized financial reporting policies and procedures and a more structured close process and (ii) implement financial data reviews that involve separate preparation and review of the monthly, quarterly and annual financial data, reconciliations, analyses and information. Based on our assessment of the additional resources and our enhanced controls and procedures, our management concluded that, as of December 31, 2013, we had remediated the material weaknesses in our internal control over financial reporting described above.

The rules governing the standards that must be met for our management to assess our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act are complex and require significant documentation, testing and possible remediation. These stringent standards require that our audit committee be advised and regularly updated on management's review of internal control over financial reporting. Our management may not be able to effectively and timely implement controls and procedures that adequately respond to the increased regulatory compliance and reporting requirements that will be applicable to us as a public company. If we fail to staff our accounting and finance function adequately or maintain internal control over financial reporting adequate to meet the demands that will be placed upon us as a public company, including the requirements of the Sarbanes-Oxley Act, our business and reputation may be harmed and our stock price may decline. Furthermore, investor perceptions of us may be adversely affected, which could cause a decline in the market price of our common stock.

***In order to satisfy our obligations as a public company, we will need to hire additional qualified accounting and financial personnel with appropriate public company experience.***

As a newly public company, we will need to establish and maintain effective disclosure and financial controls and make changes in our corporate governance practices. We will need to hire additional accounting and

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financial personnel with appropriate public company experience and technical accounting knowledge, and it may be difficult to recruit and maintain such personnel. Even if we are able to hire appropriate personnel, our existing operating expenses and operations will be impacted by the direct costs of their employment and the indirect consequences related to the diversion of management resources from product development efforts.

***Our ability to use our net operating loss carryforwards and certain tax credit carryforwards may be subject to limitation.***

As of December 31, 2013, we had federal and state net operating loss carryforwards of \$10.5 million and \$8.2 million, respectively. Our federal net operating loss carryforwards begin to expire in 2026, and our state net operating loss carryforwards begin to expire in 2014. As of December 31, 2013, we also had federal and state research and development tax credit carryforwards of \$4.7 million and \$1.3 million, respectively, which begin to expire in 2026 and 2021, respectively. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, changes in our ownership may limit the amount of our net operating loss carryforwards and research and development tax credit carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and research and development tax credit carryforwards before they expire. The completion of this offering, together with private placements and other transactions that have occurred since our inception, may trigger such an ownership change pursuant to Section 382. Any such limitation, whether as the result of this offering, prior private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us after this offering, could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study.

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

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

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

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

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### ***We may not be successful in our efforts to identify or discover additional product candidates.***

The success of our business depends primarily upon our ability to identify, develop and commercialize products based on our weight loss platform. Although beloranib is currently in clinical development, our research programs may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

### ***We may acquire businesses or products, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions.***

We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

### **Risks Related to Our Financial Position and Need for Capital**

#### ***We are a development stage biopharmaceutical company with a limited operating history and have not generated any revenue from product sales. We have incurred significant operating losses since our inception, and anticipate that we will incur continued losses for the foreseeable future.***

We are a development stage company with a limited operating history on which to base your investment decision. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We were incorporated in November 2005. Our operations to date have been limited primarily to organizing and staffing our company and conducting research and development activities for beloranib and ZGN-839. We have never generated any revenue from product sales. We have not obtained regulatory approvals for any of our product candidates.

Since our inception, we have focused substantially all of our efforts and financial resources on developing beloranib, which is currently in Phase 2 clinical development. We have funded our operations to date through proceeds from sales of redeemable convertible preferred stock and convertible debt and have incurred losses in each year since our inception. Our net losses were \$13.2 million for the year ended December 31, 2011, \$13.9 million for the year ended December 31, 2012 and \$14.0 million for the year ended December 31, 2013. As of December 31, 2013, we had a deficit accumulated during the development stage of \$68.9 million. Substantially all of our operating losses resulted from costs incurred in connection with our development program and from general and administrative costs associated with our operations. We expect to incur increasing levels of operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. We expect our research and development expenses to significantly increase in connection with our additional clinical trials of beloranib and development of ZGN-839 and of any other product candidates we may choose to pursue. In addition, if we obtain marketing approval for beloranib, we will incur significant sales, marketing and outsourced manufacturing expenses. Once we are a public company, we will incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing

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operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from our lead product candidate, beloranib, and we do not know when, or if, we will generate any revenue. We do not expect to generate significant revenue unless and until we obtain marketing approval of, and begin to sell, beloranib. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- initiate and successfully complete later-stage clinical trials that meet their clinical endpoints;
- initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for beloranib as a treatment for obesity and hyperphagia in PWS patients, craniopharyngioma-associated obesity and severely obese patients in the general population;
- commercialize beloranib, if approved, by developing a sales force or entering into collaborations with third parties; and
- achieve market acceptance of beloranib in the medical community and with third-party payors.

Absent our entering into a collaboration or partnership agreement, we expect to incur significant sales and marketing costs as we prepare to commercialize beloranib. Even if we initiate and successfully complete our pivotal clinical trials of beloranib, and beloranib is approved for commercial sale, and despite expending these costs, beloranib may not be a commercially successful drug. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate product revenue, we will not become profitable and may be unable to continue operations without continued funding.

***Even if this offering is successful, we will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.***

We are currently advancing our beloranib product candidate through clinical development. Developing small molecule products is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidate in clinical trials. Depending on the status of regulatory approval or, if approved, commercialization of beloranib, as well as the progress we make in selling beloranib, we may require additional capital to fund operating needs thereafter. We may also need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for beloranib or otherwise expand more rapidly than we presently anticipate.

As of December 31, 2013, our cash and cash equivalents were \$35.5 million. We estimate that the net proceeds from this offering will be approximately \$       million, assuming an initial public offering price of \$       per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and offering expenses payable by us. We expect that the net proceeds from this offering, together with our existing cash and cash equivalents and available borrowings under our March 2014 credit facility, will be sufficient to fund our current operations for at least the next       months. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. In any event, we will require additional capital to obtain regulatory approval for, and to commercialize, our product candidates. Raising funds in the current economic environment may present additional challenges. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.



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Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidate or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

### ***Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights.***

We may seek additional capital through a combination of private and public equity offerings, debt financings, collaborations and strategic and licensing arrangements. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, your ownership interest in our company will be diluted. In addition, the terms of any such securities may include liquidation or other preferences that materially adversely affect your rights as a stockholder. Debt financing, if available, would increase our fixed payment obligations and 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 collaboration, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable rights to beloranib, our intellectual property, future revenue streams or grant licenses on terms that are not favorable to us.

### ***If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.***

You will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Assuming an initial public offering price of \$            per share, the midpoint of the price range set forth on the cover page of this prospectus, purchasers of common stock in this offering will experience immediate dilution of \$            per share in net tangible book value of the common stock. In addition, investors purchasing common stock in this offering will contribute            % of the total amount invested by stockholders since inception but will only own            % of the shares of common stock outstanding. In the past, we issued options to acquire common stock at prices significantly below the initial public offering price. To the extent these outstanding options are ultimately exercised, investors purchasing common stock in this offering will sustain further dilution. See “Dilution” for a more detailed description of the dilution to new investors in the offering.

## **Risks Related to Our Common Stock**

### ***Market volatility may affect our stock price and the value of your investment.***

Following this offering, the market price for our common stock is likely to be volatile, in part because our common stock has not been previously traded publicly. In addition, the market price of our common stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- plans for, progress of or results from pre-clinical studies and clinical trials of beloranib;
- the failure of the FDA or the EMA to approve beloranib;
- announcements of new products, technologies, commercial relationships, acquisitions or other events by us or our competitors;
- the success or failure of other weight loss therapies;
- regulatory or legal developments in the United States and other countries;
- failure of beloranib, if approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- general market conditions and overall fluctuations in U.S. equity markets;
- variations in our quarterly operating results;
- changes in our financial guidance or securities analysts' estimates of our financial performance;
- changes in accounting principles;
- our ability to raise additional capital and the terms on which we can raise it;
- sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;
- additions or departures of key personnel;
- discussion of us or our stock price by the press and by online investor communities; and
- other risks and uncertainties described in these risk factors.

### ***An active trading market for our common stock may not develop, and you may not be able to resell your shares at or above the initial public offering price.***

Prior to this offering, there has been no public market for shares of our common stock. Although we anticipate our common stock being approved for listing on NASDAQ Global Market, an active trading market for our shares may never develop or be sustained following this offering. The initial public offering price of our common stock will be determined through negotiations between us and the underwriters. This initial public offering price may not be indicative of the market price of our common stock after this offering. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the initial public offering price or at the time that they would like to sell.

### ***Our executive officers, directors, principal stockholders and their affiliates will continue to exercise significant control over our company after this offering, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.***

Immediately following the completion of this offering, and disregarding any shares of common stock that they purchase in this offering, the existing holdings of our executive officers, directors, principal stockholders and their affiliates, including investment funds affiliated with Atlas Ventures, or Atlas, investment funds affiliated with Third Rock Ventures, or TRV, investment funds affiliated with Alta Partners, or Alta, and entities

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affiliated with Fidelity Investment, or Fidelity, will represent beneficial ownership, in the aggregate, of approximately % of our outstanding common stock, assuming no exercise of the underwriters' option to acquire additional common stock in this offering and assuming we issue the number of shares of common stock as set forth on the cover page of this prospectus. As a result, these stockholders, if they act together, will be able to influence our management and affairs and control the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. These stockholders acquired their shares of common stock for substantially less than the price of the shares of common stock being acquired in this offering, and these stockholders may have interests, with respect to their common stock, that are different from those of investors in this offering and the concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

See "Principal Stockholders" in this prospectus for more information regarding the ownership of our outstanding common stock by our executive officers, directors, principal stockholders and their affiliates.

### ***Future sales of our common stock may cause our stock price to decline.***

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

Upon completion of this offering, there will be shares of our common stock outstanding. Of these, shares are being sold in this offering (or shares, if the underwriters exercise their option in full) and will be freely tradable immediately after this offering (except for shares purchased by affiliates) and the remaining shares may be sold upon expiration of lock-up agreements six months after the date of this offering (subject in some cases to volume limitations). A large portion of these shares are held by a small number of persons and investment funds. Moreover, after this offering, Atlas, TRV, Alta, Fidelity and certain of our other stockholders will have rights, subject to some conditions, to require us to file registration statements covering the shares of our common stock they currently hold, or to include these shares in registration statements that we may file for ourselves or other stockholders. See "Description of Capital Stock—Registration Rights" in this prospectus for more information regarding these registration rights.

We also intend to register all the shares of common stock that we may issue under our equity incentive plans. Effective upon the effectiveness of the registration statement of which this prospectus is a part, an aggregate of shares of our common stock will be reserved for future issuance under these plans. Once we register these shares, which we plan to do shortly after the completion of this offering, they can be freely sold in the public market upon issuance, subject to the lock-up agreements referred to above. If a large number of these shares are sold in the public market, the sales could reduce the trading price of our common stock. See "Shares Eligible for Future Sale" for a more detailed description of sales that may occur in the future.

### ***Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.***

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the market price of our common stock could decline. Based upon the number of shares of common stock, on an as-

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converted basis, outstanding as of February 28, 2014, upon the completion of this offering, we will have outstanding a total of \_\_\_\_\_ shares of common stock, assuming no exercise of the underwriters' option to purchase additional shares. Of these shares, as of the date of this prospectus, approximately \_\_\_\_\_ shares of our common stock, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering, assuming that current stockholders do not purchase shares in this offering. The representatives of the underwriters, however, may, in their sole discretion, permit our officers, directors and other stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus. After the lock-up agreements expire, based upon the number of shares of common stock, on an as-converted basis, outstanding as of February 28, 2014, up to an additional \_\_\_\_\_ shares of common stock will be eligible for sale in the public market, \_\_\_\_\_ of which shares are held by directors, executive officers and other affiliates and will be subject to Rule 144 under the Securities Act of 1933, as amended, or the Securities Act.

In addition, as of February 28, 2014, \_\_\_\_\_ shares of common stock that are either subject to outstanding options or reserved for future issuance under our equity incentive plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

After this offering, the holders of approximately \_\_\_\_\_ shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market our common stock.

***We will have broad discretion in how we use the proceeds of this offering. We may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.***

We will have considerable discretion in the application of the net proceeds of this offering. We intend to use the net proceeds from this offering to advance the clinical development of beloranib as a treatment for obesity and hyperphagia in PWS patients and craniopharyngioma-associated obesity, to advance the clinical development of beloranib as a treatment for severe obesity in the general population, to continue the development of ZGN-839 and to fund new and ongoing research and development activities, working capital and other general corporate purposes, which may include funding for the hiring of additional personnel, capital expenditures and the costs of operating as a public company. As a result, investors will be relying upon management's judgment with only limited information about our specific intentions for the use of the balance of the net proceeds of this offering. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

***After the completion of this offering, we may be at an increased risk of securities class action litigation.***

Historically, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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***Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, even one that may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.***

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

***We are an “emerging growth company,” and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.***

We are an “emerging growth company,” as defined in the JOBS Act, and 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, 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. If we choose not to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, our auditors will not be required to attest to the effectiveness of our internal control over financial reporting. As a result, investors may become less comfortable with the effectiveness of our internal controls and the risk that material weaknesses or other deficiencies in our internal controls go undetected may increase. If we choose to provide reduced disclosures in our periodic reports and proxy statements while we are an emerging growth company, investors would have access to less information and analysis about our executive compensation, which may make it difficult for investors to evaluate our executive compensation practices. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an “emerging growth company.” We will remain an “emerging growth company” until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least \$1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30<sup>th</sup>, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

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

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which you purchased them.

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***If securities or industry analysts do not publish or cease publishing research or reports or publish misleading, inaccurate or unfavorable research about us, our business or our market, our stock price and trading volume could decline.***

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. We do not currently have and may never obtain research coverage by securities and industry analysts. If no or few securities or industry analysts cover our company, the trading price and volume of our stock would likely be negatively impacted. If we obtain securities or industry analyst coverage and if one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, or provides more favorable relative recommendations about our competitors, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price or trading volume to decline.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the sections entitled “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business,” contains forward-looking statements that are based on our management’s belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- our use of the net proceeds from this offering;
- the accuracy of our estimates regarding expenses, future revenues and capital requirements;
- our plans to develop and commercialize beloranib as a treatment for obesity that is a co-morbidity of an underlying rare condition such as PWS or craniopharyngioma, or severe obesity in the general population, or at all;
- our ability to advance beloranib into pivotal trials, and successfully complete such clinical trials;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party manufacturers and CROs;
- our ability to obtain and maintain intellectual property protection for our proprietary assets;
- the size of the potential markets for beloranib and our ability to serve those markets;
- the rate and degree of market acceptance of beloranib for any indication once approved;
- our ability to obtain additional financing;
- the success of competing products that are or become available for the indications that we are pursuing; and
- the loss of key scientific or management personnel.

In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue” or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under “Risk Factors” and elsewhere in this prospectus. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

## USE OF PROCEEDS

We estimate that our net proceeds from the sale of shares of our common stock in this offering will be approximately \$      million, or \$      million if the underwriters exercise in full their option to purchase additional shares, assuming an initial public offering price of \$      per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

A \$1.00 increase (decrease) in the assumed initial public offering price of \$      per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the net proceeds to us from this offering by \$      million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of      shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) our net proceeds from this offering by \$      million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering, plus, if needed, cash on hand, as follows:

- approximately \$      million to advance the clinical development of beloranib as a treatment for obesity and hyperphagia in PWS patients through Phase 3 clinical trials;
- approximately \$      million to advance the clinical development of beloranib as a treatment for craniopharyngioma-associated obesity through a Phase 2a clinical trial and the initiation of pivotal clinical trials;
- approximately \$      million to initiate IND-enabling studies and clinical development of ZGN-839 through the initiation of Phase 1 clinical development;
- approximately \$      million to initiate a Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population; and
- the remaining proceeds, if any, to fund new and ongoing research and development activities, working capital and other general corporate purposes.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures and the extent of clinical development may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from pre-clinical studies and any ongoing clinical trials or clinical trials we may commence in the future, as well as any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

## DIVIDEND POLICY

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



## CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of December 31, 2013:

- on an actual basis;
- on a pro forma basis, giving effect to the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into an aggregate of 94,483,404 shares of our common stock upon the completion of this offering; and
- on a pro forma as adjusted basis, giving effect to the pro forma adjustment listed above as well as the sale by us of \_\_\_\_\_ shares of our common stock in this offering at an assumed initial public offering price of \$ \_\_\_\_\_ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma as adjusted information below is illustrative only, and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table in conjunction with the sections of this prospectus entitled “Selected Consolidated Financial Data” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and with our consolidated financial statements and related notes included elsewhere in this prospectus.

	As of December 31, 2013		
	Actual	Pro Forma	Pro Forma As Adjusted(1)
	(in thousands, except share and per share data)		
Cash and cash equivalents	\$ 35,517	\$ 35,517	\$ _____
Redeemable convertible preferred stock (Series A, B, C, D and E), \$0.001 par value; 99,292,610 shares authorized, 94,483,404 issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	\$103,797	\$ —	\$ —
Stockholders’ equity (deficit):			
Preferred stock, \$0.001 par value; no shares authorized, issued or outstanding, actual; shares authorized and no shares issued or outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, \$0.001 par value; 115,000,000 shares authorized, 4,580,669 shares issued and outstanding, actual; 115,000,000 shares authorized, 99,064,073 shares issued and outstanding, pro forma; shares authorized, shares issued and outstanding, pro forma as adjusted	5	99	
Additional paid-in capital	328	104,031	
Deficit accumulated during the development stage	(68,907)	(68,907)	
Total stockholders’ equity (deficit)	(68,574)	35,223	
Total capitalization	\$ 35,223	\$ 35,223	\$ _____

- (1) A \$1.00 increase (decrease) in the assumed initial public offering price of \$ \_\_\_\_\_ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) each of cash and cash equivalents, total stockholders’ equity and total capitalization on a pro forma as adjusted basis by \$ \_\_\_\_\_ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of \_\_\_\_\_ shares in the number of shares

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offered by us, as set forth on the cover page of this prospectus, would increase (decrease) our net proceeds from this offering by \$        million, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The number of common shares shown as outstanding on a pro forma as adjusted basis in the table above is based on 4,580,669 shares of common stock outstanding as of December 31, 2013 and excludes:

- 8,228,975 shares of common stock issuable upon the exercise of outstanding options as of December 31, 2013 at a weighted average exercise price of \$0.30 per share;
- 2,331,257 shares of common stock reserved for future issuance under our 2006 Stock Option Plan as of December 31, 2013; and
- shares of our common stock reserved for future issuance under our 2014 Stock Option Plan, which will become effective upon the completion of this offering.

## DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share you will pay in this offering and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value (deficit) as of December 31, 2013 was \$(69.3) million, or \$(15.13) per share of common stock. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities and redeemable convertible preferred stock, which is not included within stockholders' equity (deficit). Historical net tangible book value per share is our historical net tangible book value (deficit) divided by the number of shares of common stock outstanding as of December 31, 2013.

Our pro forma net tangible book value as of December 31, 2013 was \$34.5 million, or \$0.35 per share of common stock. Pro forma net tangible book value represents total tangible assets less total liabilities. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares outstanding as of December 31, 2013, after giving effect to the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into an aggregate of 94,483,404 shares of our common stock upon the completion of this offering.

After giving effect to the sale by us of \_\_\_\_\_ shares of common stock in this offering at an assumed initial public offering price of \$ \_\_\_\_\_ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2013 would have been \$ \_\_\_\_\_ million, or \$ \_\_\_\_\_ per share. This represents an immediate increase in pro forma as adjusted net tangible book value of \$ \_\_\_\_\_ per share to existing stockholders and an immediate dilution of \$ \_\_\_\_\_ per share to new investors purchasing common stock in this offering at the initial public offering price. Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the assumed initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share	\$
Historical net tangible book value (deficit) per share as of December 31, 2013	\$(15.13)
Increase per share attributable to the conversion of all shares of redeemable convertible preferred stock outstanding	<u>15.48</u>
Pro forma net tangible book value per share as of December 31, 2013	0.35
Increase in pro forma as adjusted net tangible book value per share attributable to new investors purchasing shares in this offering	<u>          </u>
Pro forma as adjusted net tangible book value per share after this offering	<u>          </u>
Dilution per share to new investors participating in this offering	<u><u>\$</u></u>

A \$1.00 increase (decrease) in the assumed initial public offering price of \$ \_\_\_\_\_ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per share after this offering by \$ \_\_\_\_\_ per share and would increase (decrease) the dilution per share to new investors participating in this offering by \$ \_\_\_\_\_ per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase of \_\_\_\_\_ shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase the pro forma as adjusted net tangible book value per share after this offering by \$ \_\_\_\_\_ and decrease the dilution per share to new investors participating in this offering by \$ \_\_\_\_\_, assuming the assumed initial

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public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A share decrease in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease the pro forma as adjusted net tangible book value per share after this offering by \$ and increase the dilution per share to new investors participating in this offering by \$ , assuming the assumed initial public offering price remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. The information discussed above is illustrative only and will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

If the underwriters exercise their option to purchase additional shares in full, the pro forma as adjusted net tangible book value per share after this offering would be \$ per share, representing an increase in pro forma as adjusted net tangible book value per share to existing stockholders of \$ per share and immediate dilution in pro forma as adjusted net tangible book value per share to new investors purchasing shares in this offering of \$ per share, assuming an initial public offering price of \$ per share, the midpoint of the price range set forth on the cover page of this prospectus.

The following table summarizes, as of December 31, 2013, on a pro forma as adjusted basis described above, the number of shares of our common stock, the total consideration and the average price per share (i) paid to us by existing stockholders and (ii) to be paid by new investors purchasing shares of common stock in this offering at an assumed initial public offering price of \$ per share, the midpoint of the price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders		%	\$	%	\$
New investors					\$
Total		%	\$	%	

The table above assumes no exercise of the underwriters' option to purchase additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to % of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors participating in the offering would be increased to % of the total number of shares of our common stock outstanding after this offering.

The above discussion and tables are based on 4,580,669 shares of common stock outstanding as of December 31, 2013 and also give effect to the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into an aggregate of 94,483,404 shares of common stock upon the completion of this offering. The discussion and tables above assume no exercise of any outstanding stock options. As of December 31, 2013, there were 8,228,975 shares of common stock issuable upon exercise of outstanding options at a weighted average exercise price of \$0.30 per share. The tables above also exclude 2,331,257 shares of common stock reserved for future issuance under our 2006 Stock Option Plan as of December 31, 2013 and shares of our common stock reserved for future issuance under our 2014 Stock Option Plan, which will become effective upon the completion of this offering.

To the extent that outstanding options are exercised, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities may result in further dilution to our stockholders.

**SELECTED CONSOLIDATED FINANCIAL DATA**

You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the “Management’s Discussion and Analysis of Financial Condition and Results of Operations” section of this prospectus. We have derived the consolidated statement of operations data for the years ended December 31, 2011, 2012 and 2013 and for the cumulative period from inception (November 22, 2005) through December 31, 2013 and the consolidated balance sheet data as of December 31, 2012 and 2013 from our audited consolidated financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that should be expected in the future.

	<u>Year Ended December 31,</u>			<u>Cumulative Period</u>
	<u>2011</u>	<u>2012</u>	<u>2013</u>	<u>from Inception</u> <u>(November 22, 2005)</u> <u>to</u> <u>December 31, 2013</u>
	<u>(in thousands, except per share data)</u>			
<b>Statement of Operations Data:</b>				
Revenue	\$ —	\$ —	\$ —	\$ —
Operating expenses:				
Research and development	11,403	11,544	9,561	54,290
General and administrative	1,751	2,247	4,219	14,309
Total operating expenses	<u>13,154</u>	<u>13,791</u>	<u>13,780</u>	<u>68,599</u>
Loss from operations	<u>(13,154)</u>	<u>(13,791)</u>	<u>(13,780)</u>	<u>(68,599)</u>
Other income (expense):				
Interest income	—	—	—	120
Interest expense	—	(97)	—	(106)
Foreign currency transaction gains (losses), net	(3)	8	(247)	(243)
Total other expense, net	<u>(3)</u>	<u>(89)</u>	<u>(247)</u>	<u>(229)</u>
Net loss	<u>(13,157)</u>	<u>(13,880)</u>	<u>(14,027)</u>	<u>(68,828)</u>
Accretion of redeemable convertible preferred stock to redemption value	(53)	(67)	(213)	(554)
Net loss attributable to common stockholders	<u><u>\$ (13,210)</u></u>	<u><u>\$ (13,947)</u></u>	<u><u>\$ (14,240)</u></u>	<u><u>\$ (69,382)</u></u>
Net loss per share attributable to common stockholders, basic and diluted <sup>(1)</sup>	<u><u>\$ (3.05)</u></u>	<u><u>\$ (3.13)</u></u>	<u><u>\$ (3.11)</u></u>	
Weighted average common shares outstanding, basic and diluted <sup>(1)</sup>	<u><u>4,327</u></u>	<u><u>4,457</u></u>	<u><u>4,578</u></u>	
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited) <sup>(2)</sup>			<u><u>\$ (0.17)</u></u>	
Pro forma weighted average common shares outstanding, basic and diluted (unaudited) <sup>(2)</sup>			<u><u>84,190</u></u>	

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	As of December 31,	
	2012	2013
	(in thousands)	
<b>Balance Sheet Data:</b>		
Cash and cash equivalents	\$ 9,935	\$ 35,517
Working capital <sup>(3)</sup>	7,394	34,443
Total assets	10,986	38,138
Redeemable convertible preferred stock	62,785	103,797
Total stockholders' deficit	(54,729)	(68,574)

- (1) See Note 9 to our consolidated financial statements for further details on the calculation of basic and diluted net loss per share attributable to common stockholders.
- (2) See Note 9 to our consolidated financial statements for further details on the calculation of basic and diluted pro forma net loss per share attributable to common stockholders.
- (3) We define working capital as current assets less current liabilities.

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

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

### Overview

We are a biopharmaceutical company dedicated to significantly improving the health and well-being of patients affected by obesity. Beloranib, our lead product candidate, is a novel, first-in-class, twice-weekly subcutaneous injection being developed for the treatment of multiple indications, including obesity and hyperphagia, or insatiable life-threatening hunger and hunger-related behaviors, in Prader-Willi Syndrome, or PWS, craniopharyngioma-associated obesity, and severe obesity in the general population.

PWS is a rare and complex genetic disorder characterized by physiologic, cognitive and behavioral symptoms, including hyperphagia, and severe obesity. We recently completed two Phase 2a clinical trials evaluating beloranib's ability to reduce body weight and to improve hyperphagia, one in PWS patients and one in severely obese patients. In our Phase 2a clinical trials, we observed reductions in body weight, body mass and body fat content in both patient populations and reductions in hyperphagia-related behaviors in PWS patients. In January 2013, the U.S. Food and Drug Administration, or FDA, granted orphan designation for our application to treat PWS with beloranib. We plan to initiate a Phase 3 clinical program, consisting of two Phase 3 clinical trials, of beloranib in PWS patients in 2014 after finalizing the program design based on conversations with the FDA and certain European regulatory authorities. We filed an application to obtain orphan drug designation for beloranib as a treatment for PWS in the European Union in early 2014. We believe that rare conditions such as PWS afford us an opportunity to rapidly develop and commercialize beloranib using smaller, more focused and less costly clinical trials, relative to those required to develop beloranib for the broader severe obesity population.

Obesity is a complex medical disorder involving appetite dysregulation and altered lipid and energy metabolism that results in excessive accumulation of fat tissue. Weight loss and hunger control are urgently needed for certain subpopulations of obese patients, such as those with PWS and craniopharyngioma, whose obesity is life-threatening and a co-morbidity of an underlying condition. These conditions are characterized by uncontrollable hunger resulting from damage to or impaired functioning of the hypothalamus, an area of the brain responsible for many functions including the desire to eat. Published population studies estimate that the prevalence of PWS in the United States and in the European Union ranges from 1 in 8,000 to 1 in 50,000. The physiological drive to eat in PWS patients is so powerful that they will go to great lengths to eat large quantities of food, even if it is spoiled, indigestible or unpalatable to others. Unsupervised patients will often eat to the point that it causes serious physical harm or death. As a result, caregivers are often forced to place locks and alarms on refrigerators and pantries that contain food. Despite attempts to control the access to food, the typical adult PWS patient is morbidly obese and, based on our evaluation of published survival data, has an average life expectancy of 32 years of age. Unfortunately, neither dietary intervention nor currently available pharmaceutical therapies bring meaningful benefit to PWS patients and, as a result, they experience severe and life-threatening consequences of their condition. Furthermore, existing surgical techniques such as bariatric surgery are contraindicated in PWS, as PWS patients often overeat to a point whereby they can rupture their stomachs, which is frequently a cause of death. Since beloranib works through a novel mechanism that does not appear to require a fully functioning hypothalamic control pathway, we believe that obese patients with conditions in which increased hunger is central to the disease may respond well to treatment with beloranib.

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We are pursuing clinical development of beloranib as a treatment for severely obese patients in the general population, including patients otherwise eligible for bariatric surgery. Bariatric surgery eligibility criteria generally identify surgical candidates as those patients with body mass indices, or BMIs, greater than 40 kg/m<sup>2</sup>, or those with BMIs over 35 kg/m<sup>2</sup> who also have a significant and uncontrolled co-morbid condition. Based on these criteria, it is estimated conservatively that there will be at least 16 million adults in the United States eligible for bariatric surgery by the time beloranib or another methionine aminopeptidase 2, or MetAP2, inhibitor could become available commercially. Bariatric surgery results in significant weight loss, but the financial expense and the potential for complications, adverse events and longer-term side effects limit its overall adoption, with only a few hundred thousand patients in the United States undergoing bariatric surgery each year. Existing pharmacotherapies result in less weight loss than surgical options, and these therapies not only have undesirable side effects, but also have risk of abuse. Due to the significant barriers associated with bariatric surgery and the limited weight loss potential of currently marketed pharmaceutical products, there is a significant unmet need for the treatment of patients with severe obesity. We believe this patient population would benefit from MetAP2 inhibitor treatment through the reduction of body weight and through improvement of other co-morbid conditions. In 2013, we completed a 12-week Phase 2a clinical trial of beloranib administered twice weekly in obese patients. We observed placebo-adjusted weight loss, or weight loss observed beyond that seen in the control arm, of up to 10.3% after 12 weeks of treatment with beloranib. In addition, we observed reductions in levels of low density lipoprotein cholesterol, C-reactive protein and systolic blood pressure. Patients treated with beloranib also reported reduced hunger, as assessed using a visual analog scale, a widely used self-reported measure of hunger and related endpoints. We intend to initiate a Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population. We are also evaluating additional proprietary MetAP2 inhibitors beyond beloranib as potential development candidates that would provide increased patient convenience in the form of oral dosing, or an otherwise improved clinical profile. A decision on whether to subsequently advance beloranib into pivotal trials for severe obesity or to leverage the opportunity to advance another MetAP2 inhibitor into early development for severe obesity is anticipated to be made on the basis of results obtained from our planned Phase 3 clinical program of beloranib in PWS patients and discussions with regulatory authorities. MetAP2 inhibitors may also have utility in the treatment of other metabolic diseases, such as nonalcoholic steatohepatitis, or NASH, and type 2 diabetes. In a mouse model of diabetes and NASH, our second product candidate, ZGN-839, a MetAP2 inhibitor, reduced the severity of NASH and reduced plasma glucose.

Since our inception in November 2005, we have devoted substantially all of our resources to developing beloranib and ZGN-839, building our intellectual property portfolio, developing the supply chain, business planning, raising capital, and providing general and administrative support for these operations. To date, we have funded our operations primarily through sales of redeemable convertible preferred stock and, to a lesser extent, through the issuances of convertible promissory notes. From our inception through December 31, 2013, we have received gross proceeds of \$103.6 million from such transactions.

We are a development stage company and have not generated any revenue. We have incurred net losses in each year since our inception, and we have a deficit accumulated during the development stage of \$68.9 million as of December 31, 2013. Our net losses were \$13.2 million, \$13.9 million and \$14.0 for the years ended December 31, 2011, 2012 and 2013, respectively. These losses have resulted principally from costs incurred in connection with in-licensing our product candidates, research and development activities and general and administrative costs associated with our operations. We expect to incur significant expenses and increasing operating losses for the foreseeable future.

We expect that our expenses will increase substantially in connection with our ongoing activities, as we:

- advance the clinical development of beloranib as a treatment for obesity and hyperphagia in PWS patients through our Phase 3 clinical program;
- advance the clinical development of beloranib as a treatment for craniopharyngioma-associated obesity through a Phase 2a clinical trial and the initiation of pivotal clinical trials;



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- initiate Investigational New Drug Application, or IND, enabling studies and clinical development of ZGN-839 and our second-generation MetAP2 inhibitors through the initiation of Phase 1 clinical development;
- initiate a Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population;
- seek to identify additional indications for beloranib;
- seek to obtain regulatory approvals for our product candidates;
- add operational, financial and management information systems;
- add personnel, including personnel to support our product development and future commercialization; and
- maintain, leverage and expand our intellectual property portfolio.

As a result, we will need additional financing to support our continuing operations. Until such time that we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity or debt financings or other sources, which may include collaborations with third parties. Arrangements with collaborators or others may require us to relinquish rights to certain of our technologies or product candidates. In addition, we may never successfully complete development of any of our product candidates, obtain adequate patent protection for our technology, obtain necessary regulatory approval for our product candidates or achieve commercial viability for any approved product candidates. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We will need to generate significant revenue to achieve profitability, and we may never do so.

We expect that our existing cash and cash equivalents as of December 31, 2013 and available borrowings under our March 2014 credit facility, together with anticipated net proceeds from this offering, will enable us to fund our operating expenses and capital expenditures requirements for at least months. See “—Liquidity and Capital Resources.”

## **Financial Operations Overview**

### ***Revenue***

We have not generated any revenue from product sales since our inception, and do not expect to generate any revenue from the sale of products in the near future. If our development efforts result in clinical success and regulatory approval or collaboration agreements with third parties for our product candidates, we may generate revenue from those product candidates.

### ***Operating Expenses***

The majority of our operating expenses since inception have consisted primarily of in-licensing costs of our product candidate beloranib, research and development activities, and general and administrative costs.

#### *Research and Development Expenses*

Research and development expenses, which consist primarily of costs associated with our product research and development efforts, are expensed as incurred. Research and development expenses consist primarily of:

- personnel costs, including salaries, related benefits and stock-based compensation for employees engaged in scientific research and development functions;
- third-party contract costs relating to research, formulation, manufacturing, pre-clinical studies and clinical trial activities;

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- external costs of outside consultants;
- payments made under our third-party licensing agreements;
- laboratory consumables; and
- allocated facility-related costs.

We have been developing beloranib, ZGN-839, and our second-generation MetAP2 inhibitors, and typically use our employee, consultant and infrastructure resources across our development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, external consultant costs, payments made under our licensing agreements or other internal costs to specific development programs or product candidates. We record our research and development expenses net of any research and development tax incentives we are entitled to receive from government authorities.

The following table summarizes our research and development expenses by program:

	<u>Year Ended December 31,</u>			<u>Cumulative Period</u>
	<u>2011</u>	<u>2012</u>	<u>2013</u>	<u>from Inception</u>
	<u>(in thousands)</u>			<u>(November 22, 2005)</u>
				<u>to December 31,</u>
				<u>2013</u>
Beloranib	\$ 5,523	\$ 6,802	\$5,881	\$ 26,036
ZGN-839 and other early-stage development	2,332	2,193	295	11,052
Unallocated expenses	3,548	2,549	3,385	17,202
Total research and development expenses	<u>\$11,403</u>	<u>\$11,544</u>	<u>\$9,561</u>	<u>\$ 54,290</u>

Research and development activities are central to our business. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to increase in the foreseeable future as we pursue later stages of clinical development of our product candidates.

We cannot determine with certainty the duration and completion costs of the current or future clinical trials of our product candidates or if, when, or to what extent we will generate revenue from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs, and timing of clinical studies and development of our product candidates will depend on a variety of factors, including:

- the scope, rate of progress, and expense of our ongoing as well as any additional clinical trials and other research and development activities;
- future clinical trial results;
- uncertainties in clinical trial enrollment rate or design;
- significant and changing government regulation; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

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### *General and Administrative Expenses*

General and administrative expenses consist primarily of personnel costs, consisting of salaries, related benefits and stock-based compensation, of our executive, finance, business and corporate development and other administrative functions. General and administrative expenses also include travel expenses, allocated facility-related costs not otherwise included in research and development expenses, and professional fees for auditing, tax and legal services, including legal expenses to pursue patent protection of our intellectual property.

We expect that general and administrative expenses will increase in the future as we expand our operating activities and incur additional costs associated with operating as a public company. These public company related increases will likely include additional costs related to personnel; legal, accounting and audit services; directors' and officers' liability insurance premiums; and investor relations.

### *Other Income (Expense)*

*Interest income.* Interest income consists of interest earned on our cash and cash equivalents. Our interest income has not been significant due to low interest earned on invested balances. We anticipate that our interest income will increase in the future due to increased balances from the receipt of proceeds from our sales of Series E redeemable convertible preferred stock in November 2013 and anticipated cash proceeds from this offering.

*Interest expense.* Interest expense consists of interest expense on our outstanding convertible promissory notes at the stated interest rates and interest expense related to the amortization of deferred financing costs associated with our issuances of the convertible promissory notes. As of December 31, 2012, all of our outstanding convertible promissory notes and accrued interest had been converted into shares of our redeemable convertible preferred stock. As a result, we will no longer incur interest expense related to this debt.

*Foreign currency transaction gains (losses), net.* Foreign currency transaction gains (losses), net consists of the realized and unrealized gains and losses from foreign currency-denominated cash balances, vendor payables and tax-related receivables from the Australian government. We currently do not engage in hedging activities related to our foreign currency-denominated receivables and payables; as such, we cannot predict the impact of future foreign currency transaction gains and losses on our operating results. See "—Quantitative and Qualitative Disclosures about Market Risk."

### *Income Taxes*

Since our inception in 2005, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items. As of December 31, 2013, we had federal and state net operating loss carryforwards of \$10.5 million and \$8.2 million, respectively. Our federal net operating loss carryforwards begin to expire in 2026, and our state net operating loss carryforwards begin to expire in 2014. We also had federal and state research and development tax credit carryforwards of \$4.7 million and \$1.3 million, respectively, as of December 31, 2013, which begin to expire in 2026 and 2021, respectively.

### **Critical Accounting Policies and Significant Judgments and Estimates**

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States of America. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. We believe that the estimates and assumptions involved in the accounting policies described below may have the greatest potential impact on our consolidated financial statements and, therefore, consider these to be our critical accounting policies. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions. See also Note 2 of our consolidated financial statements included elsewhere in this prospectus for information about these critical accounting policies as well as a description of our other significant accounting policies.

### ***JOBS Act***

On April 5, 2012, the Jumpstart Our Business Startups Act, or the JOBS Act, was signed into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an “emerging growth company.” As an “emerging growth company,” we are electing not to take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards and, as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Section 107 of the JOBS Act provides that our decision not to take advantage of the extended transition period is irrevocable.

In addition, we are in the process of evaluating the benefits of relying on the other exemptions and reduced reporting requirements provided by the JOBS Act. Subject to certain conditions set forth in the JOBS Act, if as an “emerging growth company” we choose to rely on such exemptions, we may not be required to, among other things, (i) provide an auditor’s attestation report on our system of internal controls over financial reporting pursuant to Section 404, (ii) provide all of the compensation disclosure that may be required of non-emerging growth public companies under the Dodd-Frank Wall Street Reform and Consumer Protection Act, (iii) comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements (auditor discussion and analysis), and (iv) disclose certain executive compensation-related items such as the correlation between executive compensation and performance and comparisons of the Chief Executive Officer’s compensation to median employee compensation. These exemptions will apply for a period of five years following the completion of our initial public offering or until we no longer meet the requirements of being an “emerging growth company,” whichever is earlier.

### ***Research and Development Expenses***

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- contract research organizations, or CROs, in connection with clinical trials;
- investigative sites or other providers in connection with clinical trials;
- vendors in connection with pre-clinical development activities; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the

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status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

### ***Stock-Based Compensation***

We measure stock-based awards granted to employees and directors at fair value on the date of grant and recognize the corresponding compensation expense of those awards, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. Generally, we issue stock options and restricted stock awards with only service-based vesting conditions and record the expense for these awards using the straight-line method. We have historically granted stock options with exercise prices equivalent to the fair value of our common stock as of the date of grant.

We measure stock-based awards granted to consultants and nonemployees at the fair value of the award on the date at which the related service is complete. Compensation expense is recognized over the period during which services are rendered by such consultants and nonemployees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is re-measured using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

The fair value of each stock option grant is estimated using the Black-Scholes option-pricing model. We historically have been a private company and lack company-specific historical and implied volatility information. Therefore, we estimate our expected volatility based on the historical volatility of our publicly traded peer companies and expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded stock price. The expected term of our options has been determined utilizing the “simplified” method for awards that qualify as “plain-vanilla” options, while the expected term of our options granted to consultants and nonemployees has been determined based on the contractual term of the options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

The assumptions we used to determine the fair value of stock options granted to employees and directors are as follows, presented on a weighted average basis (we did not grant any stock options to employees or directors during the year ended December 31, 2012):

	Year Ended December 31,	
	2011	2013
Risk-free interest rate	1.41%	1.12%
Expected term (in years)	6.25	6.25
Expected volatility	78%	85%
Expected dividend yield	0%	0%

These assumptions represented our best estimates, but the estimates involve inherent uncertainties and the application of our judgment. As a result, if factors change and we use significantly different assumptions or estimates, our stock-based compensation expense could be materially different. We recognize compensation expense for only the portion of awards that are expected to vest. In developing a forfeiture rate estimate for pre-vesting forfeitures, we have considered our historical experience of actual forfeitures. If our future actual forfeiture rate is materially different from our estimate, our stock-based compensation expense could be significantly different from what we have recorded in the current period.

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The following table summarizes the classification of our stock-based compensation expenses recognized in our consolidated statements of operations:

	Year Ended December 31,		
	2011	2012	2013
	(in thousands)		
Research and development	\$ 30	\$ 68	\$ 176
General and administrative	50	53	219
	<u>\$ 80</u>	<u>\$ 121</u>	<u>\$ 395</u>

### *Valuations of Common Stock*

The fair value of our common stock is determined on each date of grant by our board of directors, with input from management, and considers our most recently available valuation of common stock and our assessment of additional objective and subjective factors that we believe are relevant and which may change from the date of the most recent valuation through the date of the grant. In the absence of a public trading market for our common stock, our determination of the fair value of our common stock was performed using methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants Audit and Accounting Practice Aid Series: *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. In addition, our board of directors considered various objective and subjective factors, along with input from management, to determine its best estimate of the fair value of our common stock as of each grant date, including the following:

- contemporaneous third-party valuations of our common stock;
- the prices at which we sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to our common stock;
- the progress of our research and development programs, including the status of clinical trials for our product candidates;
- our stage of development and business strategy;
- our financial condition, including cash on hand;
- our historical and forecasted performance and operating results;
- the composition of, and changes to, our management team and board of directors;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event such as a sale of our company or an initial public offering, or IPO, given prevailing market conditions;
- the analysis of initial public offerings and the market performance of similar companies in the biopharmaceutical industry;
- external market conditions affecting the biopharmaceutical industry; and
- trends within the biopharmaceutical industry.

### *Valuation Methodologies*

Our common stock valuations have been prepared utilizing either the option-pricing method, or OPM, or a hybrid of the OPM and the probability-weighted expected return method, or PWERM.

The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a

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company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceed the value of the preferred stock liquidation preference at the time of a liquidity event, such as a strategic sale, merger or IPO. The common stock is modeled as a call option on the underlying equity value at a predetermined exercise price. In the model, the exercise price is based on a comparison with the total equity value rather than, as in the case of a regular call option, a comparison with a per share stock price. Thus, common stock is considered to be a call option with a claim on the enterprise at an exercise price equal to the remaining value immediately after the preferred stock liquidation preference is paid.

The OPM uses the Black-Scholes option-pricing model to price the call options. This model defines the securities' fair values as functions of the current fair value of a company and uses assumptions such as the anticipated timing of a potential liquidity event and the estimated volatility of the equity securities. The aggregate value of the common stock derived from the OPM is then divided by the number of shares of common stock outstanding to arrive at the per share value.

The OPM backsolve approach was used to estimate enterprise value under the OPM. The OPM backsolve approach uses the OPM to calculate the implied equity value based on recent sales of the company's securities. In the OPM, the assumed volatility factor was based on the historical trading volatility of our publicly traded peer companies. At each valuation date, a determination was made by us as to the appropriate volatility to be used, considering such factors as the expected time to a liquidity event and our stage of development.

To derive the fair value of the common stock using the OPM, the proceeds to the common stockholders were calculated based on the preferences and priorities of the preferred and common stock, including the participation features of certain series of the preferred stock. We then applied a discount for lack of marketability to the common stock to account for the lack of access to an active public market.

Under the PWERM methodology, the fair value of common stock is estimated based upon an analysis of future values for the company, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. We then applied a discount for lack of marketability to the common stock to account for the lack of access to an active public market.

In the hybrid PWERM and OPM, two valuation approaches were used to estimate enterprise value: the market approach and the OPM backsolve approach. Under the market approach, we estimated enterprise value using the guideline public company method, which includes comparisons to publicly traded companies in the relevant industry that recently completed IPOs. The enterprise value is then discounted back to the valuation date at an appropriate risk-adjusted discount rate.

In the hybrid PWERM and OPM, two types of future event scenarios were considered: an IPO and a sale transaction. The IPO scenario was valued using either the OPM backsolve approach or the guideline public company method. The sale scenario was valued using the OPM backsolve approach. The relative probability of each type of future event scenario was determined by our board of directors based on an analysis of market conditions at the time, including then-current IPO valuations of similarly situated companies, and expectations as to the timing and likely prospects of the future-event scenarios.

To derive the fair value of the common stock for each scenario using the hybrid PWERM and OPM, the proceeds to the common stockholders were calculated based on the preferences and priorities of the preferred and common stock. We then applied a discount for lack of marketability to the common stock to account for the lack of access to an active public market.

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### *Common Stock Valuations*

*July 31, 2011 Valuation.* To aid in the determination of the fair value of our common stock, a third-party valuation analysis was prepared as of July 31, 2011 using the OPM. In determining the enterprise value, we applied the OPM backsolve approach to calculate our implied equity value based on the pricing of our Series C preferred stock financing at \$0.91 per share in June 2011. We estimated the time to liquidity as 2.0 years based on the then-current plans and estimates of our board of directors and management regarding our likely need to raise additional capital within this timeframe. We assumed volatility of 86% based on historical trading volatility of our publicly traded peer companies. We used a risk-free rate of return of 0.36%, based on the two-year U.S. Treasury yield curve. We then applied a discount for lack of marketability of 35%. The July 31, 2011 analysis resulted in a valuation of our common stock of \$0.25 per share.

*January 31, 2013 Valuation.* To aid in the determination of the fair value of our common stock, a third-party valuation analysis was prepared as of January 31, 2013. Based upon our determination that in late 2012 an IPO had become a possible but uncertain liquidity event, the valuation was prepared using the hybrid PWERM and OPM, which considered a sale scenario and an IPO scenario. For those two future-event scenarios, management and our board of directors determined that the probability of the sale scenario was 85% and the probability of the IPO scenario was 15%, based on our assessment of our development pipeline and market conditions. In determining the enterprise value for the sale scenario, we applied the OPM backsolve approach to calculate our implied equity value based on the pricing of our Series D preferred stock financing at \$1.36 per share in November 2012 and January 2013 and considering the participating nature of the preferred stock in a sale scenario and the expected time to a sale. In determining the enterprise value for the IPO scenario, we applied the OPM backsolve approach to calculate our implied equity value based on the pricing of our Series D preferred stock financing at \$1.36 per share in November 2012 and January 2013 and considering the convertible nature of the preferred stock in an IPO scenario and the expected time to an IPO. For purposes of the January 31, 2013 valuation, we also estimated that the time to completion of a sale transaction was 1.5 years and the time to completion of an IPO was 1.0 year. For the sale and IPO scenarios, we assumed volatility of 67% and 53%, respectively, based on the trading volatilities of our publicly traded peer companies for our expected time to liquidity of each scenario. We then applied a discount for lack of marketability of 25% under each of the sale and IPO scenarios. The January 31, 2013 analysis resulted in a valuation of our common stock of \$0.39 per share.

*June 30, 2013 Valuation.* To aid in the determination of the fair value of our common stock, a third-party valuation analysis was prepared as of June 30, 2013 using the hybrid PWERM and OPM, which considered an IPO scenario and a sale scenario. For those two future-event scenarios, management and our board of directors determined that the probability of each scenario was 50%, based on our assessment of our development pipeline, market conditions and progress towards undertaking an IPO. In determining the enterprise value for the IPO scenario, we applied the guideline public company method under the market approach, which considered the increase in value that occurred from the most recent preferred financing round to the IPO for a group of biopharmaceutical companies that had completed IPOs in the preceding two years. In determining the enterprise value for the sale scenario, we applied the OPM backsolve approach to calculate our implied equity value, using a \$2.00 estimated price per share and the rights and preferences of Series E preferred stock in a planned preferred stock financing expected to close in late 2013. For purposes of the June 30, 2013 valuation, we also estimated that the time to completion of an IPO was 0.58 year and the time to completion of a sale transaction was 1.75 years. Our estimate of the time to a liquidity event in a sale transaction increased from our estimate used in the January 31, 2013 valuation due to our reassessment of potential sale transactions and current market conditions. For the IPO scenario, we applied a risk-adjusted discount rate of 30% to the value of common stock. For the sale scenario, we assumed volatility of 68%, based on the trading volatilities of our publicly traded peer companies for our expected time to liquidity. We then applied a discount for lack of marketability of 10% under each of the IPO and sale scenarios. The June 30, 2013 analysis resulted in a valuation of our common stock of \$1.08 per share.

*December 20, 2013 Valuation.* To aid in the determination of the fair value of our common stock, a third-party valuation analysis was prepared as of December 20, 2013 using the hybrid PWERM and OPM, which



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considered an IPO scenario, a short-term sale scenario and a long-term sale scenario. For those three future-event scenarios, management and our board of directors determined that the probability of the IPO scenario was 60%, the probability of a short-term sale scenario was 10% and the probability of a long-term sale scenario was 30%. These probabilities were based on our assessment of our development pipeline, market conditions and progress towards undertaking an IPO. In determining the enterprise value for the IPO scenario, we applied the guideline public company method under the market approach, which considered the increase in value that occurred from the most recent preferred financing round to the IPO for a group of biopharmaceutical companies that had completed IPOs in the preceding two years. In determining the enterprise value for the two sale scenarios, we applied the OPM backsolve approach to calculate our implied equity value, using the \$2.17 price per share and the rights and preferences of the recently completed Series E preferred stock financing that closed in November 2013. For purposes of the December 20, 2013 valuation, we also estimated that the time to completion of an IPO was 0.42 years and the time to completion of a short-term and long-term sale transaction was 0.75 years and 3.0 years, respectively. For the IPO scenario, we applied a risk-adjusted discount rate of 25% to the value of common stock. For the short-term and long-term sale scenarios, we assumed volatility of 65% and 74%, respectively, based on the trading volatilities of our publicly traded peer companies for our expected time to liquidity. We then applied a discount for lack of marketability of 5% under the IPO scenario, 10% under the short-term sale scenario and 15% under the long-term sale scenario. The December 20, 2013 analysis resulted in a valuation of our common stock of \$1.54 per share.

### *Option Grants*

The following table summarizes by grant date the number of shares subject to options granted between January 1, 2012 and February 3, 2014, the per share exercise price of the options, the fair value of common stock underlying the options on date of grant, and the per share estimated fair value of the options:

<b>Grant Date</b>	<b>Number of Shares Subject to Options Granted</b>	<b>Per Share Exercise Price of Options<sup>(1)</sup></b>	<b>Fair Value of Common Stock on Date of Option Grant</b>	<b>Per Share Estimated Fair Value of Options<sup>(2)</sup></b>
February 28, 2012 (nonemployee award)	50,000	\$ 0.25	\$ 0.25	\$ 0.20 <sup>(3)</sup>
March 7, 2013	4,344,748	\$ 0.39	\$ 0.39	\$ 0.28
October 3, 2013	10,000	\$ 1.08	\$ 1.08	\$ 0.79
October 3, 2013 (nonemployee award)	110,000	\$ 1.08	\$ 1.08	\$ 0.88 <sup>(3)</sup>
December 20, 2013	50,000	\$ 1.54	\$ 1.54	\$ 1.15
January 30, 2014	1,250,000	\$ 1.54	\$ 1.54	\$ 1.16
February 3, 2014	25,000	\$ 1.54	\$ 1.54	\$ 1.16

- (1) The Per Share Exercise Price of Options represents the determination by our board of directors of the fair value of our common stock on the date of grant, as determined taking into account our most recently available valuation of common stock as well as additional factors, which may have changed since the date of the most recent contemporaneous valuation through the date of grant.
- (2) The Per Share Estimated Fair Value of Options reflects the weighted average fair value of options granted on each grant date as estimated at the date of grant using the Black-Scholes option-pricing model. This model estimates the fair value using as inputs the exercise price of the option and assumptions of the risk-free interest rate, expected term of the option, expected share price volatility of the underlying common stock, expected dividends on the underlying common stock, and the per share fair value of the underlying common stock.
- (3) For the purposes of recording stock-based compensation for grants of options to nonemployees, we measure the fair value of options on the service completion date (vesting date). At the end of each reporting period prior to completion of the services, we re-measure the value of the unvested portion of the outstanding options at the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

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Our board of directors determined the fair value of common stock on each option grant date based on a variety of factors. We determined that the fair value of our common stock increased from \$0.25 per share as of January 1, 2012 to \$1.54 as of February 3, 2014. The following discussion describes the reasons for the increases in the fair value of our common stock over this period and as compared to the midpoint of the price range set forth on the cover page of this prospectus of \$      per share.

*Year Ended December 31, 2012.* Our board of directors determined that the fair value of our common stock was \$0.25 per share as of October 11, 2011. We believe that the fair value of our common stock remained unchanged through February 28, 2012, when we granted stock options for the purchase of 50,000 shares of common stock to a consultant. During the period from October 11, 2011 through February 28, 2012, we continued to operate our business in the ordinary course. At that time, our lead product candidate beloranib was in early-stage Phase 1b clinical trials, while our other product candidates were in earlier stages of development. In February 2012, we closed the final round of Series C preferred stock financing at \$0.91 per share, which matched the price per share paid in our initial issuance of Series C redeemable convertible preferred stock in June 2011. Over this period, we had no plans for an initial public offering in the near term because we did not believe that the public markets presented a favorable environment for a biopharmaceutical company at our stage of development.

In the third quarter of 2012, we initiated a 12-week Phase 2a clinical trial of beloranib in Australia. This clinical trial was important in that beloranib was being studied as a longer-term treatment to show that weight loss would continue past the four weeks previously studied and, for the first time, it was studied in males and patients with diabetes. In November 2012, we executed a Series D preferred stock financing, under which we issued shares to a new investor in November 2012 at \$1.36 per share and committed to issue shares to existing investors in January 2013 at \$1.36 per share. In late 2012, we started to consider whether the markets presented a favorable environment for an IPO for a biopharmaceutical company at our stage of development; however, we did not have any definitive plans to pursue an IPO at that time. We believed that the fair value of our common stock increased to \$0.39 per share as of December 31, 2012, based on our board of directors' determination of the fair value of our common stock as of March 7, 2013.

*Year Ended December 31, 2013.* During the first quarter of 2013, we continued to operate our business in the ordinary course. There were no significant developments in our clinical trials or in our research and development efforts as our Phase 2a clinical trial of beloranib in Australia was ongoing. In January 2013, we received orphan drug designation for beloranib for the treatment of PWS and also completed our scheduled closing of Series D redeemable convertible preferred stock. In February 2013, we obtained a third-party valuation of our common stock as of January 31, 2013 as one of the factors considered by our board of directors in its determination of the fair value of our common stock. That valuation considered an IPO scenario for the first time as we determined that an IPO had become a possible but uncertain liquidity event and resulted in an estimated fair value of our common stock of \$0.39 per share. While we were considering a possible IPO at that time, we did not believe that the markets would be favorable to us for an IPO until we had results from our Phase 2a clinical trial of beloranib for severe obesity. Our board of directors determined that the fair value of common stock was \$0.39 per share as of March 7, 2013. We believed that the fair value of our common stock remained unchanged through March 31, 2013.

In April 2013, we filed an IND with the FDA for beloranib to be tested in patients with PWS. In May 2013, we started to receive results from our recently completed Phase 2a clinical trial of beloranib in severely obese patients, which showed rapid, progressive and sustained clinically meaningful body weight loss. Additionally, in June 2013, we initiated a Phase 2a clinical trial in patients with PWS, evaluating beloranib for its ability to reduce body weight and to improve hyperphagia, a condition characterized by increased hunger and hunger-related behaviors. During the second quarter of 2013, we evaluated the public market environment and determined that the market conditions were favorable for biopharmaceutical companies. Those favorable market conditions and positive results from our Phase 2a clinical trial of beloranib in severely obese patients enabled us to pursue an IPO. In June and July 2013, we met with investment bankers to discuss a potential IPO, and we began to engage lawyers and accountants to assist us in preparation for an IPO. In early-August 2013, we obtained a third-party valuation of our common stock as of June 30, 2013 as one of the factors to be considered

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by our board of directors in its determination of the fair value of our common stock. In that valuation, we adjusted our model to account for the increased probability of an IPO scenario, in light of continued favorable market conditions and our progress achieved towards a potential IPO of our common stock. Based on the revised valuation model and the changes in our business and in the market values of biopharmaceutical companies, as well as the impact on our common stock of our increasing enterprise value, we determined that the fair value of our common stock had increased to \$1.08 per share as of June 30, 2013.

During the third quarter of 2013, we continued to operate our business in the ordinary course. There were no significant developments in our clinical trials or in our research and development efforts as our Phase 2a clinical trial evaluating beloranib in PWS patients was ongoing. While we continued to meet with investment bankers and continued to carry out activities related to preparation for a potential IPO, we determined that we would need results from our Phase 2a clinical trial of beloranib in patients with PWS before we could engage investment bankers for an IPO. As a result of these factors, we believed that the fair value of our common stock remained unchanged at \$1.08 per share through September 30, 2013.

During the fourth quarter of 2013, we continued to operate our business in the ordinary course. Our board of directors determined that the fair value of our common stock remained at \$1.08 per share as of October 3, 2013. Later in October, we started to receive initial results from our ongoing Phase 2a clinical trial of beloranib in patients with PWS. In late October 2013, we engaged investment bankers, in anticipation of receiving final results from the PWS Phase 2a clinical trial completed in the fourth quarter and being able to pursue an IPO shortly thereafter. We held our initial IPO organizational meeting in November 2013. We also executed a Series E preferred stock financing, under which we issued shares to new investors in late November 2013 at \$2.17 per share, raising net proceeds of \$34.8 million. In December 2013, we obtained a third-party valuation of our common stock as one of the factors considered by our board of directors in its determination of the fair value of our common stock as of December 20, 2013. We adjusted our valuation model to account for the increased probability of an IPO scenario, in light of continued favorable market conditions, favorable results from our Phase 2a clinical trial of beloranib in patients with PWS and our progress achieved towards a potential IPO of our common stock. Based on the revised valuation model and the changes in our business and in the market values of biopharmaceutical companies, as well as the impact on our common stock of our increasing enterprise value, our board of directors determined that the fair value of our common stock had increased to \$1.54 per share as of December 20, 2013. We believed that the fair value of our common stock remained unchanged through December 31, 2013.

*January 1, 2014 through February 3, 2014.* Through February 3, 2014, we continued to operate our business in the ordinary course. On January 31, 2014, we submitted to the SEC a confidential draft registration statement for an IPO as contemplated by our board of directors in its determination of the fair value of our common stock as of December 20, 2013. Our board of directors determined that the fair value of our common stock remained unchanged at \$1.54 per share as of January 30, 2014. We believe that the fair value of our common stock remained unchanged through February 3, 2014.

[Table of Contents](#)**Results of Operations****Comparison of Years Ended December 31, 2012 and 2013**

The following table summarizes our results of operations for the years ended December 31, 2012 and 2013:

	Year Ended December 31,		Increase (Decrease)
	2012	2013	
	(in thousands)		
Revenue	\$ —	\$ —	\$ —
Operating expenses:			
Research and development	11,544	9,561	(1,983)
General and administrative	2,247	4,219	1,972
Total operating expenses	13,791	13,780	(11)
Loss from operations	(13,791)	(13,780)	11
Other income (expense):			
Interest expense	(97)	—	97
Foreign currency transaction gains (losses), net	8	(247)	(255)
Total other expense, net	(89)	(247)	(158)
Net loss	<u>\$ (13,880)</u>	<u>\$ (14,027)</u>	<u>\$ (147)</u>

**Research and development expenses**

	Year Ended December 31,		Increase (Decrease)
	2012	2013	
	(in thousands)		
Direct research and development expenses by program:			
Beloranib:			
Pre-clinical and manufacturing	\$ 4,365	\$ 2,898	\$ (1,467)
Clinical trials	2,437	2,983	546
Subtotal	6,802	5,881	(921)
ZGN-839 and other early-stage development	2,193	295	(1,898)
Subtotal	8,995	6,176	(2,819)
Unallocated expenses:			
Personnel related	902	1,258	356
Consultants	1,371	1,981	610
Licensing, milestone and license maintenance fees	150	—	(150)
Other	126	146	20
Subtotal	2,549	3,385	836
Total research and development expenses	<u>\$11,544</u>	<u>\$9,561</u>	<u>\$ (1,983)</u>

Research and development expenses for the year ended December 31, 2012 were \$11.5 million, compared to \$9.6 million for the year ended December 31, 2013. The decrease of \$1.9 million was primarily due to the decreased costs of \$1.9 million associated with ZGN-839 and other early-stage development programs (consisting of our second-generation MetAP2 inhibitors) and decreased costs of \$0.9 million associated with beloranib, partially offset by an increase in consultant expenses of \$0.6 million and an increase in personnel related costs of \$0.4 million. During 2013, we focused our research and development efforts primarily on our ongoing clinical trials for beloranib as opposed to our early-stage programs. Expenses related to beloranib decreased year over year as a result of a \$1.5 million decrease in pre-clinical and manufacturing expenses,

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partially offset by an increase of \$0.5 million from our clinical trial expenses. Pre-clinical and manufacturing costs decreased year over year as a result of completing a significant portion of our development-enabling toxicology and other pre-clinical activities related to beloranib in 2012. Clinical trial expenses for beloranib increased by \$0.5 million year over year as a result of expenses incurred for our 12-week Phase 2a clinical trial for severe obesity and for our 12-week Phase 2a clinical trial for PWS that were both ongoing in 2013, as compared to expenses incurred for our 12-week Phase 2a clinical trial for severe obesity that started in 2012 and for our 4-week Phase 1b clinical trial for severe obesity that was started and completed in 2012. Expenses for our Phase 2a clinical trial for severe obesity, which ran from the third quarter of 2012 through the second quarter of 2013, were recorded net of a 45% research and development tax incentive from the Australian government of \$0.6 million and \$1.2 million during the years ended December 31, 2012 and 2013, respectively. Consultant costs increased by \$0.6 million year over year primarily due to expenses incurred in conjunction with our IND filing for our Phase 2a clinical trial for PWS. Personnel related costs increased by \$0.4 million year over year primarily due to the hiring of a new employee of \$0.2 million and increased stock-based compensation of \$0.1 million.

### *General and administrative expenses*

	Year Ended December 31,		Increase (Decrease)
	2012	2013	
	(in thousands)		
Personnel related	\$ 910	\$1,358	\$ 448
Professional fees	947	2,463	1,516
Travel and other	390	398	8
Total general and administrative expenses	<u>\$2,247</u>	<u>\$4,219</u>	<u>\$ 1,972</u>

General and administrative expenses for the year ended December 31, 2012 were \$2.2 million, compared to \$4.2 million for the year ended December 31, 2013. The increase of \$2.0 million in general and administrative expenses was primarily due to increased professional fees of \$1.5 million and increased personnel related costs of \$0.4 million year over year. The increase in professional fees consisted primarily of a \$1.0 million increase in accounting and audit, legal and investor relations fees due to ongoing business activities as well as an increase of \$0.4 million related to two external market research studies that were conducted in 2013. Personnel related costs increased by \$0.4 million year over year primarily due to employee salary and bonus increases of \$0.2 million and increases in stock-based compensation of \$0.2 million.

### *Other income (expense), net*

*Interest expense.* Interest expense for the year ended December 31, 2012 was related to interest on convertible promissory notes issued in August 2012 that were subsequently converted into shares of our Series D redeemable convertible preferred stock in November 2012. We had no debt outstanding during 2013.

*Foreign currency transaction gains (losses), net.* Net foreign currency transaction losses of \$0.2 million for the year ended December 31, 2013 were primarily due to the re-measurement of receivables, denominated in Australian dollars, from the Australian government for research and development tax incentives, reflecting both a strengthening of the U.S. dollar relative to the Australian dollar and an increase in our receivable balances for such tax incentives during the year ended December 31, 2013.

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**Comparison of Years Ended December 31, 2011 and 2012**

The following table summarizes our results of operations for the years ended December 31, 2011 and 2012:

	Year Ended December 31,		Increase (Decrease)
	2011	2012	
	(in thousands)		
Revenue	\$ —	\$ —	\$ —
Operating expenses:			
Research and development	11,403	11,544	141
General and administrative	1,751	2,247	496
Total operating expenses	<u>13,154</u>	<u>13,791</u>	<u>637</u>
Loss from operations	(13,154)	(13,791)	(637)
Other income (expense):			
Interest expense	—	(97)	(97)
Foreign currency transaction gains (losses), net	(3)	8	11
Total other expense, net	<u>(3)</u>	<u>(89)</u>	<u>(86)</u>
Net loss	<u>\$ (13,157)</u>	<u>\$ (13,880)</u>	<u>\$ (723)</u>

**Research and development expenses**

	Year Ended December 31,		Increase (Decrease)
	2011	2012	
	(in thousands)		
Direct research and development expenses by program:			
Beloranib:			
Pre-clinical and manufacturing	\$ 4,533	\$ 4,365	\$ (168)
Clinical trials	990	2,437	1,447
Subtotal	<u>5,523</u>	<u>6,802</u>	<u>1,279</u>
ZGN-839 and other early-stage development	<u>2,332</u>	<u>2,193</u>	<u>(139)</u>
Subtotal	<u>7,855</u>	<u>8,995</u>	<u>1,140</u>
Unallocated expenses:			
Personnel related	590	902	312
Consultants	1,749	1,371	(378)
Licensing, milestone and license maintenance fees	1,055	150	(905)
Other	154	126	(28)
Subtotal	<u>3,548</u>	<u>2,549</u>	<u>(999)</u>
Total research and development expenses	<u>\$ 11,403</u>	<u>\$ 11,544</u>	<u>\$ 141</u>

Research and development expenses for the year ended December 31, 2011 were \$11.4 million, compared to \$11.5 million for the year ended December 31, 2012. The increase of \$0.1 million was primarily due to the increased costs of \$1.3 million associated with our beloranib product candidate and increased personnel related costs of \$0.3 million, partially offset by a decrease of \$0.9 million in licensing, milestone and license maintenance fees, a decrease of \$0.4 million in consultant expenses, and a decrease of \$0.1 million in costs associated with ZGN-839 and other early-stage development programs, consisting of our second-generation MetAP2 inhibitors. Expenses related to beloranib increased year over year as a result of a \$1.4 million increase from our clinical trial expenses, partially offset by a decrease of \$0.2 million in pre-clinical and manufacturing. Clinical trial expenses for beloranib increased by \$1.4 million year over year as a result of expenses incurred for our 4-week Phase 1b clinical trial for severe obesity that was started and completed in 2012 and our 12-week Phase 2a clinical trial for severe obesity that

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we commenced in the third quarter of 2012, as compared to expenses incurred solely for our 4-week Phase 1b clinical trial for severe obesity that was completed during 2011. Expenses for our Phase 2a clinical trial for severe obesity incurred in the fourth quarter of 2012 were recorded net of a 45% research and development tax incentive from the Australian government of \$0.6 million. There were no research and development tax incentives recorded during the year ended December 31, 2011. Pre-clinical and manufacturing costs associated with beloranib decreased primarily as a result of decreased drug product costs. Personnel related costs increased by \$0.3 million year over year primarily due to increased headcount as a result of the addition of our Chief Medical Officer in September 2011, which had the effect of decreasing consultant expense by a similar amount. Licensing, milestone and license maintenance fees decreased by \$0.9 million year over year due primarily to the recognition of a \$1.0 million milestone payment in 2011.

### *General and administrative expenses*

	Year Ended December 31,		Increase (Decrease)
	2011	2012	
	(in thousands)		
Personnel related	\$ 925	\$ 910	\$ (15)
Professional fees	527	947	420
Travel and other	299	390	91
Total general and administrative expenses	<u>\$1,751</u>	<u>\$2,247</u>	<u>\$ 496</u>

General and administrative expenses for the year ended December 31, 2011 were \$1.8 million compared to \$2.2 million for the year ended December 31, 2012. The increase of \$0.4 million was primarily attributable to increased professional fees of \$0.4 million related to ongoing business activities.

### *Other income (expense), net*

*Interest expense.* Interest expense for the year ended December 31, 2012 was due to interest on convertible promissory notes issued in August 2012 and November 2012 that were subsequently converted into shares of Series D redeemable convertible preferred stock in November 2012. We had no debt outstanding during 2011.

*Foreign currency transaction gains (losses), net.* We had a small amount of foreign currency transaction losses during the year ended December 31, 2011 compared to a small amount of foreign currency transaction gains during the year ended December 31, 2012. Foreign currency transaction gains and losses related primarily to the re-measurement of foreign currency accounts and foreign currency denominated vendor payables.

## **Liquidity and Capital Resources**

Since our inception in November 2005, we have not generated any revenue and have incurred recurring net losses. As of December 31, 2013, we had a deficit accumulated during the development stage of \$68.9 million. We have funded our operations since inception primarily through sales of redeemable convertible preferred stock and, to a lesser extent, through the issuances of convertible promissory notes. From our inception through December 31, 2013, we have received gross proceeds of \$103.6 million from such transactions.

As of December 31, 2013, we had cash and cash equivalents totaling \$35.5 million. We invest our cash equivalents in money market accounts in order to preserve principal.

On March 31, 2014, we entered into a loan and security agreement, or the 2014 Credit Facility, which provides for initial borrowings of \$7.5 million and additional borrowings of up to \$12.5 million. On that same date, we received proceeds of \$7.5 million from the issuance of promissory notes under a term loan as part of the facility. Of the additional \$12.5 million of borrowings available to us, \$7.5 million is available to be drawn down until September 30, 2014 and \$5.0 million is available subject to our completion of an initial public offering with net cash proceeds to us of at least \$50.0 million, or a Qualified IPO. Upon a Qualified IPO, that additional \$5.0 million will be available to be drawn down through the earlier of December 31, 2014 or 30 days after the Qualified IPO. All promissory notes issued under the 2014 Credit Facility are due on December 1, 2017 and are collateralized by substantially all of our personal property, other than our intellectual property. There are no

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financial covenants associated with the debt facility; however, there are negative covenants restricting our activities, including limitations on dispositions, mergers or acquisitions; encumbering or granting a security interest in our intellectual property; incurring indebtedness or liens; paying dividends; making certain investments; and certain other business transactions.

Under the 2014 Credit Facility, we are obligated to make monthly, interest-only payments on any term loans funded under the facility until December 1, 2014 and, thereafter, to pay 36 consecutive, equal monthly installments of principal and interest from January 1, 2015 through December 1, 2017. Upon a Qualified IPO, the term of monthly, interest-only payments will be extended until June 1, 2015. Term loans under the 2014 Credit Facility bear interest at an annual rate of 8.1%. In addition, a final payment equal to 6.0% of any amounts drawn under the facility is due upon the earlier of the maturity date, acceleration of the term loans or prepayment of all or part of the term loans. We are also obligated to pay a separate fee of up to \$0.5 million upon any initial public offering; a sale of substantially all of our assets; or a merger, reorganization or sale of our voting equity securities where existing voting stockholders hold less than 50% of voting equity securities after such transaction.

The following table summarizes our sources and uses of cash for each of the periods presented below:

	Year Ended December 31,		
	2011	2012	2013
	(in thousands)		
Cash used in operating activities	\$(12,274)	\$(13,589)	\$(15,004)
Cash used in investing activities	(45)	(2)	(17)
Cash provided by financing activities	10,069	22,059	40,603
Net increase (decrease) in cash and cash equivalents	<u>\$ (2,250)</u>	<u>\$ 8,468</u>	<u>\$ 25,582</u>

### *Net cash used in operating activities*

During the year ended December 31, 2011, operating activities used \$12.3 million of cash, primarily resulting from our net loss of \$13.2 million, partially offset by cash provided from changes in our operating assets and liabilities of \$0.8 million. Our net loss was primarily attributed to research and development activities related to our beloranib and ZGN-839 programs and our general and administrative expenses, as we had no revenue in the period. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2011 consisted primarily of an increase in accrued expenses of \$0.9 million. Our accrued expense balances were affected by the timing of vendor invoicing and payments.

During the year ended December 31, 2012, operating activities used \$13.6 million of cash, primarily resulting from our net loss of \$13.9 million, partially offset by non-cash charges of \$0.2 million and by cash provided from changes in our operating assets and liabilities of \$0.1 million. Our net loss was primarily attributed to research and development activities related to our beloranib and ZGN-839 programs and our general and administrative expenses, as we had no revenue in the period. Our net non-cash charges during the year ended December 31, 2012 primarily consisted of stock-based compensation expense of \$0.1 million and non-cash interest expense of \$0.1 million. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2012 consisted primarily of a \$1.0 million increase in accounts payable and accrued expenses, partially offset by a \$0.6 million increase in our research and development tax incentive receivable from the Australian government and a \$0.3 million increase in prepaid expenses and other current assets. Our prepaid expenses and other current assets, accounts payable and accrued expense balances were affected by the timing of vendor invoicing and payments.

During the year ended December 31, 2013, operating activities used \$15.0 million of cash, resulting from our net loss of \$14.0 million and from cash used by changes in our operating assets and liabilities of \$1.6 million, partially offset by non-cash charges of \$0.7 million. Our net loss was primarily attributed to research and development activities related to our beloranib program and our general and administrative expenses, as we had no revenue in the period. Net cash used by changes in our operating assets and liabilities during the year ended December 31, 2013 consisted primarily of a \$1.2 million increase in our research and development tax incentive receivable from the Australian government. Our net non-cash charges in the year primarily consisted of stock-based compensation expense of \$0.4 million and unrealized foreign currency transaction losses of \$0.3 million. Unrealized



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foreign currency transaction losses related to our outstanding foreign currency-denominated research and development tax incentive receivable from the Australian government.

### *Net cash used in investing activities*

We used a small amount of cash during the years ended December 31, 2011, 2012 and 2013 related to purchases of property and equipment. During the year ended December 31, 2011, we also paid a small deposit related to our office lease which we expect to be returned at the completion of the lease.

### *Net cash provided by financing activities*

During the year ended December 31, 2011, net cash provided by financing activities was \$10.1 million as a result of net proceeds raised from issuances of our Series B redeemable convertible preferred stock and Series C redeemable convertible preferred stock.

During the year ended December 31, 2012, net cash provided by financing activities was \$22.1 million. Net cash provided by financing activities primarily resulted from net proceeds of \$16.1 million raised from issuances of our Series C redeemable convertible preferred stock and Series D redeemable convertible preferred stock and net proceeds of \$6.0 million from the issuance of convertible promissory notes.

During the year ended December 31, 2013, net cash provided by financing activities was \$40.6 million as a result of net proceeds of \$6.0 million from issuances of our Series D redeemable convertible preferred stock and \$34.8 million from issuances of our Series E redeemable convertible preferred stock, partially offset by payments of \$0.2 million of deferred offering costs in anticipation of our proposed initial public offering that we expect to complete in 2014.

Beloranib is still in clinical development and ZGN-839 and our second-generation MetAP2 inhibitors are in pre-clinical development. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- advance the clinical development of beloranib as a treatment for obesity and hyperphagia in PWS patients through Phase 3 clinical trials;
- advance the clinical development of beloranib as a treatment for craniopharyngioma-associated obesity through a Phase 2a clinical trial and the initiation of pivotal clinical trials;
- initiate IND-enabling studies and clinical development of ZGN-839 and our second-generation MetAP2 inhibitors through the initiation of Phase 1 clinical development;
- initiate a Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population;
- seek to identify additional indications for beloranib;
- seek to obtain regulatory approvals for our product candidates;
- add operational, financial and management information systems;
- add personnel, including personnel to support our product development and future commercialization; and
- maintain, leverage and expand our intellectual property portfolio.

We expect that the net proceeds from this offering, together with our existing cash and cash equivalents as of December 31, 2013 and available borrowings under our March 2014 credit facility, will enable us to fund our operating expenses and capital expenditures requirements for at least months. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of beloranib, ZGN-839 and our second-generation MetAP2 inhibitors and because the extent to which we may enter into collaborations with third parties for development of these product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements for beloranib, ZGN-839 and our second-generation MetAP2 inhibitors will depend on many factors, including:

- the costs, timing and outcome of regulatory review;

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- the costs of future research and development activities, including clinical trials;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other products and technologies; and
- our ability to establish any future collaboration arrangements on favorable terms, if at all.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt 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 and may require the issuance of warrants, which could potentially dilute your ownership interest. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs of beloranib, ZGN-839 or our second-generation MetAP2 inhibitors 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 beloranib, ZGN-839 or our second-generation MetAP2 inhibitors that we would otherwise prefer to develop and market ourselves.

Since our inception in 2005, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items. As of December 31, 2013, we had federal and state net operating loss carryforwards of \$10.5 million and \$8.2 million, respectively. Our federal net operating loss carryforwards begin to expire in 2026, and our state net operating loss carryforwards begin to expire in 2014. As of December 31, 2013, we also had federal and state research and development tax credit carryforwards of \$4.7 million and \$1.3 million, respectively, which begin to expire in 2026 and 2021, respectively. We have not completed a study to assess whether an ownership change, generally defined as a greater than 50% change (by value) in the equity ownership of our corporate entity over a three-year period, has occurred or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such studies. Accordingly, our ability to utilize our tax carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be utilized against future taxes. As a result, we may not be able to take full advantage of these carryforwards for federal and state tax purposes.

### Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2013 and the effect such obligations are expected to have on our liquidity and cash flow in future periods:

Total	Payments Due By Period			
	Less Than 1 Year	1- 3 Years	3- 5 Years	More Than 5 years
Operating lease commitments <sup>(1)</sup>	\$ 64	\$ —	\$ —	\$ —
Total <sup>(2) (3)</sup>	\$ 64	\$ —	\$ —	\$ —

- (1) We lease office space in Cambridge, Massachusetts under an operating lease agreement that initially expired on July 31, 2013, but was amended in 2013 to extend the lease through January 31, 2014, with an opportunity to extend for up to two six-month periods. We have extended the lease pursuant to the terms of the first extension option, under which the lease expires on July 31, 2014 and is cancellable upon 30 days' notice.
- (2) We have acquired exclusive rights to develop patented compounds and related know-how under licensing agreements for beloranib with two third parties. The licensing rights obligate us to make payments to the licensors for license fees, milestones, license maintenance fees and royalties. We are also responsible for patent prosecution

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costs. We are obligated to make future milestone payments under these agreements of up to \$19.0 million upon achieving certain pre-commercialization milestones, such as clinical trials and government approvals, and up to \$12.5 million upon achieving certain product commercialization milestones. In addition, under one of the license agreements, we are obligated to pay up to \$1.3 million with respect to each subsequent licensed product, if any, that is a new chemical entity. We reasonably anticipate that we may be required to pay \$6.7 million of milestone payments in 2014, provided various development milestones are achieved. Amounts related to contingent milestone payments are not considered contractual obligations as they are contingent on the successful achievement of certain milestones. These milestones may not be achieved. Because the achievement of these milestones has not occurred as of December 31, 2013, no liabilities for such contingencies have been recorded in our consolidated financial statements. In addition, we will owe single-digit royalties on sales of commercial products developed using these licensed technologies, if any. We are obligated to pay to the licensors a percentage of fees received if and when we sublicense the technologies. As of December 31, 2013, we have not yet developed a commercial product using the licensed technologies and we have not entered into any sublicense agreements for the technologies.

- (3) We enter into contracts in the normal course of business with CROs for clinical trials, pre-clinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts generally provide for termination upon notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

### **Off-Balance Sheet Arrangements**

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under Securities and Exchange Commission rules, such as relationships with unconsolidated entities or financial partnerships, which are often referred to as structured finance or special purpose entities, established for the purpose of facilitating financing transactions that are not required to be reflected on our balance sheets.

### **Recently Issued Accounting Pronouncements**

Accounting standards that have been issued or proposed by the Financial Accounting Standards Board or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on our consolidated financial statements upon adoption.

### **Quantitative and Qualitative Disclosure about Market Risk**

#### ***Interest Rate Fluctuation Risk***

Our cash and cash equivalents as of December 31, 2013 consisted of cash and money market accounts. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of the instruments in our portfolio, a sudden change in market interest rates would not be expected to have a material impact on our financial condition and/or results of operation.

#### ***Foreign Currency Exchange Risk***

Foreign currency transaction exposure results primarily from transactions with our contract research organizations and other providers related to our clinical trials that are denominated in currencies other than the functional currency of the legal entity in which the transaction is recorded by us, primarily the Australian dollar. Any transaction gains or losses resulting from currency fluctuations is recorded on a separate line in our consolidated statement of operations. Net foreign currency transaction losses of \$0.2 million were recorded for the year ended December 31, 2013.

Currently, our largest foreign currency exposures are those with respect to the Australian dollar. Relative to foreign currency exposures existing as of December 31, 2013, a 10% unfavorable movement in foreign currency exchange rates would expose us to losses in earnings. For the year ended December 31, 2013, we estimated that a 10% unfavorable movement in foreign currency exchange rates would have increased our net loss by \$0.2 million. This amount is based on a sensitivity analysis performed on our financial position as of December 31, 2013. We have experienced and we will continue to experience fluctuations in our net income (loss) as a result of revaluing our assets and liabilities that are not denominated in the functional currency of the entity that recorded the asset or liability. At this time, we do not hedge our foreign currency risk.

## BUSINESS

### Overview

We are a biopharmaceutical company dedicated to significantly improving the health and well-being of patients affected by obesity. Beloranib, our lead product candidate, is a novel, first-in-class, twice-weekly subcutaneous injection being developed for the treatment of multiple indications, including obesity and hyperphagia, or insatiable life-threatening hunger and hunger-related behaviors, in Prader-Willi Syndrome, or PWS, craniopharyngioma-associated obesity, and severe obesity in the general population.

PWS is a rare and complex genetic disorder characterized by physiologic, cognitive and behavioral symptoms, including hyperphagia and obesity. We recently completed two Phase 2a clinical trials evaluating beloranib's ability to reduce body weight and to improve hyperphagia, one in PWS patients and one in severely obese patients. In our Phase 2a clinical trials, we observed reductions in body weight, body mass and body fat content in both patient populations and reductions in hyperphagia-related behaviors in PWS patients. In January 2013, the U.S. Food and Drug Administration, or FDA, granted orphan designation for our application to treat PWS with beloranib. We plan to initiate a Phase 3 clinical program, consisting of two Phase 3 clinical trials, of beloranib in PWS patients in 2014 after finalizing the program design based on conversations with the FDA and certain European regulatory authorities. We filed an application to obtain orphan drug designation for beloranib as a treatment for PWS in the European Union in early 2014. We believe that rare conditions such as PWS afford us an opportunity to rapidly develop and commercialize beloranib using smaller, more focused and less costly clinical trials, relative to those required to develop beloranib for the broader severe obesity population.

Obesity is a complex medical disorder involving appetite dysregulation and altered lipid and energy metabolism that results in excessive accumulation of fat tissue. Weight loss and hunger control are urgently needed for certain subpopulations of obese patients, such as those with PWS and craniopharyngioma, whose obesity is life-threatening and a co-morbidity of an underlying condition. These conditions are characterized by uncontrollable hunger resulting from damage to or impaired functioning of the hypothalamus, an area of the brain responsible for many functions including the desire to eat. Published population studies estimate that the prevalence of PWS in the United States and in the European Union ranges from 1 in 8,000 to 1 in 50,000. The physiological drive to eat in PWS patients is so powerful that they will go to great lengths to eat large quantities of food, even if it is spoiled, indigestible or unpalatable to others. Unsupervised patients will often eat to the point that it causes serious physical harm or death. As a result, caregivers are often forced to place locks and alarms on refrigerators and pantries that contain food. Despite attempts to control the access to food, the typical adult PWS patient is morbidly obese and, based on our evaluation of published survival data, has an average life expectancy of 32 years of age. Unfortunately, neither dietary intervention nor currently available pharmaceutical therapies bring meaningful benefit to PWS patients and, as a result, they experience severe and life-threatening consequences of their condition. Furthermore, existing surgical techniques such as bariatric surgery are contraindicated in PWS, as PWS patients often overeat to a point whereby they can rupture their stomachs, which is frequently a cause of death. Since beloranib works through a novel mechanism that does not appear to require a fully functioning hypothalamic control pathway, we believe that obese patients with conditions in which increased hunger is central to the disease may respond well to treatment with beloranib.

Zafgen was founded in 2005 to explore novel approaches to obesity therapeutics, including agents known to inhibit methionine aminopeptidase 2, or MetAP2, that had been found to drive unprecedented weight loss and metabolic improvements in mice. After performing a wide range of experiments to validate the effects of MetAP2 inhibitors in validated animal models, we committed the full resources of the company to testing the efficacy and safety of MetAP2 inhibition in obese patients and to establishing the feasibility of MetAP2 inhibitors for eventual commercialization. This effort led to our initiation of medicinal chemistry efforts to identify novel MetAP2 inhibitors, and to search for compounds that were more advanced in clinical development. We identified beloranib as a suitable in-licensing candidate, and, in parallel with preparing beloranib for use in otherwise healthy but obese patients, we conducted our own chemistry program to identify compounds with complementary characteristics. After completing studies to establish preliminary safety, mechanism of action, manufacturing feasibility and clinical proof of concept, we advanced beloranib as a clinical

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development candidate and explored its application in severely obese patient populations. Our early clinical experience highlighted several key aspects of beloranib's actions, including rapid and robust weight loss, changes in circulating hormones known to impact fat metabolism, clinically significant reductions in cardiovascular disease risk markers and a particularly striking impact on hunger. These benefits may be of particular relevance to patients suffering from severe obesity and life-limiting obesity driven by other underlying conditions, and for whom existing therapies fail to bring needed benefits.

We are pursuing clinical development of beloranib as a treatment for severely obese patients in the general population, including patients otherwise eligible for bariatric surgery. Bariatric surgery eligibility criteria generally identify surgical candidates as those patients with body mass indices, or BMIs, greater than 40 kg/m<sup>2</sup>, or those with BMIs over 35 kg/m<sup>2</sup> who also have a significant and uncontrolled co-morbid condition. Based on these criteria, it is estimated conservatively that there will be at least 16 million adults in the United States eligible for bariatric surgery by the time beloranib or another MetAP2 inhibitor could become available commercially. Bariatric surgery results in significant weight loss, but the financial expense and the potential for complications, adverse events and longer-term side effects limit its overall adoption, with only a few hundred thousand patients in the United States undergoing bariatric surgery each year. Existing pharmacotherapies result in less weight loss than surgical options, and these therapies not only have undesirable side effects, but also have risk of abuse. Due to the significant barriers associated with bariatric surgery and the limited weight loss potential of currently marketed pharmaceutical products, there is a significant unmet need for the treatment of patients with severe obesity. We believe this patient population would benefit from MetAP2 inhibitor treatment through the reduction of body weight and through improvement of other co-morbid conditions.

In 2013, we completed a 12-week Phase 2a clinical trial of beloranib administered twice weekly in obese patients. We observed placebo-adjusted weight loss, or weight loss observed beyond that seen in the control arm, of up to 10.3% after 12 weeks of treatment with beloranib. In addition, we observed reductions in levels of low density lipoprotein cholesterol, C-reactive protein and systolic blood pressure. Patients treated with beloranib also reported reduced hunger, as assessed using a visual analog scale, a widely used self-reported measure of hunger and related endpoints. We intend to initiate a Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population. We are also evaluating additional proprietary MetAP2 inhibitors beyond beloranib as potential development candidates that would provide increased patient convenience in the form of oral dosing, or an otherwise improved clinical profile. A decision on whether to subsequently advance beloranib into pivotal trials for severe obesity or to leverage the opportunity to advance another MetAP2 inhibitor into early development for severe obesity is anticipated to be made on the basis of results obtained from our planned Phase 3 clinical trial of beloranib in PWS patients and discussions with regulatory authorities. MetAP2 inhibitors may also have utility in the treatment of other metabolic diseases, such as nonalcoholic steatohepatitis, or NASH, and type 2 diabetes. In a mouse model of diabetes and NASH, our second product candidate, ZGN-839, a MetAP2 inhibitor, reduced the severity of NASH and reduced plasma glucose.

Beloranib is a novel, first-in-class injectable small molecule therapy with a unique mechanism of action that reduces hunger while stimulating the use of stored fat as an energy source. Beloranib is the first anti-obesity agent with the potential to address two important abnormalities that are present in the obese patient—hunger that is inappropriate relative to the amount of energy stored as fat and dysregulation of fat metabolism, which causes more fat to be made and stored in an obese patient than in a lean person. Beloranib acts through potent inhibition of MetAP2, an enzyme that modulates the activity of key cellular processes that control metabolism. MetAP2 inhibitors work, at least in part, by directing MetAP2 binding to cellular stress mediators, thereby reducing the tone of signals that drive lipid synthesis by the liver and fat storage throughout the body. In this manner, MetAP2 inhibition serves the purpose of re-establishing balance to the ways the body packages and metabolizes fat and glucose. MetAP2 inhibitors reduce the production of new fatty acid molecules by the liver and help convert stored fats into useful energy, while reducing hunger.

We have completed five clinical trials, including two Phase 2a clinical trials, evaluating beloranib in over 200 patients. Although these clinical trials were of short duration and designed to demonstrate safety and tolerability, significant decreases in both body weight and sense of hunger were observed in patients treated with beloranib when compared to the placebo group.

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Additional clinical trials of longer-term treatment with beloranib designed to demonstrate efficacy are required before we can submit an NDA for beloranib as a treatment for any indication that we are pursuing. In our planned Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population and our planned Phase 3 clinical program of beloranib as a treatment for PWS patients, patients will be treated with beloranib for a substantially longer period of time than as treated in our earlier clinical trials. In addition, we observed improvements in cardiovascular disease risk factors such as plasma total cholesterol, low density lipoprotein cholesterol and C-reactive protein. Across our completed clinical trials, beloranib has been well-tolerated at doses in the range of 1.0 mg to 2.0 mg administered twice weekly, and has not been associated with serious side effects. Laboratory safety measures, vital signs and electrocardiograms have been unremarkable in all completed clinical trials for all doses of beloranib tested.

## Product Pipeline

The following table summarizes our product pipeline and development status of our product candidates for the treatment of indications we are currently pursuing:

<u>Indication</u>	<u>Product Candidate</u>	<u>Stage of Development</u>	<u>Development Status</u>
Obesity and hyperphagia in PWS patients	Beloranib	Phase 2a	<ul style="list-style-type: none"><li>•Phase 2a clinical trial completed</li><li>•Phase 2a clinical trial report expected to be ready in the second quarter of 2014</li><li>•Phase 3 clinical program design being finalized and expected to begin in 2014, pending input from regulatory authorities</li></ul>
Craniopharyngioma-associated obesity	Beloranib	Phase 2a	<ul style="list-style-type: none"><li>•Phase 2a clinical trial expected to start in the first half of 2014</li></ul>
Severe obesity in the general population	Beloranib	Phase 2a	<ul style="list-style-type: none"><li>•Phase 2a clinical trial completed</li><li>•Phase 2b clinical trial expected to begin in the second half of 2014</li><li>•Advancement into pivotal trials under consideration</li><li>•Development candidates under consideration</li></ul>
	Second-generation MetAP2 inhibitors	Pre-clinical	
Nonalcoholic steatohepatitis, or NASH, nonalcoholic fatty liver disease, abdominal obesity and type 2 diabetes	ZGN-839	Pre-clinical	<ul style="list-style-type: none"><li>•Pre-clinical studies ongoing</li><li>•Investigational New Drug Application, or IND, filing anticipated by the first half of 2015</li></ul>

## Populations of Interest

### *Obesity Caused by Rare Conditions*

Obesity is a complex medical disorder involving appetite dysregulation and altered lipid and energy metabolism that results in excessive accumulation of fat tissue. We initially plan to develop beloranib for the treatment of subpopulations of obese patients, including those with rare conditions such as PWS and craniopharyngioma, where obesity is a co-morbidity of an underlying condition. These conditions frequently are characterized by increased and life-threatening hunger that occurs secondary to damage to the hypothalamus, genetic conditions affecting embryological development or function of the hypothalamus, or conditions that occur as a result of certain drug side effects, radiation therapy, or other impairments to the normal function of the hypothalamus. Regardless of the causative agent or condition, the resultant damage to the hypothalamus impairs its normal function, including the ability to modulate hunger. These conditions are most often associated with a severe and life-limiting form of obesity and neither dietary interventions nor currently available pharmaceutical therapies bring meaningful benefit to these patients, for whom bariatric surgery is generally contra-indicated. Based on results from animal experiments in which compromised hypothalamic function caused hunger and obesity, we believe that beloranib may have utility in the treatment of severe obesity and hyperphagia, or excess

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hunger, in human disease settings in which hypothalamic food intake control centers are compromised. We are developing beloranib in these subpopulations of patients as a treatment for obesity and hyperphagia in PWS patients and craniopharyngioma-associated obesity, and are continuing to explore the use of beloranib as a treatment for severe obesity in the general population.

### *PWS*

PWS is the most common known genetic cause of life-threatening obesity. PWS is a rare and complex non-inherited genetic disorder, which results from abnormalities of the fifteenth chromosome. Symptoms associated with PWS are believed to result, in part, from a defect in the hypothalamus, an important supervisory center in the brain that controls many important bodily functions, such as hunger, metabolism of fats and carbohydrates, regulation of the sleep-wake cycle and expression of emotions.

Beginning in childhood, the brain of a PWS patient fails to regulate metabolism and appetite normally. As a result, the vast majority of PWS patients suffer from hyperphagia and obesity. PWS patients are constantly preoccupied with food and an unrelenting and overriding physiological drive to eat. Hyperphagia, a leading symptom of PWS, has a significant negative impact on the patients' quality of life as well as drives obesity and a range of associated co-morbidities. Normal satiety, or the feeling of fullness after eating, does not exist in a person with PWS. The physiological drive to eat is so powerful and overwhelming that most PWS patients will go to great lengths to eat large quantities of food, even if it is spoiled, indigestible, or unpalatable to others. Furthermore, PWS patients have a reduced propensity for nausea and vomiting. In addition to obesity, a variety of other symptoms can be associated with PWS, including cognitive challenges, intellectual disabilities, growth hormone deficiency/short stature, low sensitivity to pain, hypersomnolence, or excessive sleepiness, and infertility due to hypogonadism, or insufficient production of sex hormones.

Hyperphagia impairs the PWS patients' ability to live independently, requiring costly and constant supervision to prevent overeating. Without supervision, PWS patients are likely to die prematurely as a result of choking, stomach rupture or tissue necrosis, or from complications caused by morbid obesity, such as right heart failure and respiratory failure. Based on our evaluation of published survival data, the average life expectancy of PWS patients is approximately 32 years of age. While a small number of PWS patients are cared for in costly group homes, the majority of PWS patients are cared for in their homes and their families undertake substantial effort to create physical barriers to eating. These efforts result in extremely stressful environments as caregivers often place locks and alarms on cabinets and refrigerators that contain food to impede PWS patients' efforts to obtain food at all times. We estimate the typical annual cost of treating a PWS patient is \$100,000 to \$200,000, excluding the often significant costs of drug therapies related to other medical and psychological conditions, and the costs of any lost time from work experienced by their families due to responsibilities related to the care of a PWS patient.

Published population studies estimate that the prevalence of PWS in the United States and in the European Union ranges from 1 in 8,000 to 1 in 50,000. PWS is diagnosed at an early age, typically in the first year of life, and we believe that, due to the severity of the condition and its unique attributes, the vast majority of patients affected by PWS are diagnosed. Approximately 50% of PWS patients are 13 years of age or older. We believe that further information regarding the prevalence of PWS will become available through a patient registry that is currently being developed by the Foundation for Prader-Willi Research.

Although there are pharmacological treatments for various symptoms of PWS, such as replacement of human growth hormone in PWS patients that are deficient in growth hormone, based on our discussions with physicians who treat PWS patients, there are currently no effective pharmacological treatments for obesity and hyperphagia in PWS. Furthermore, bariatric surgery is contraindicated in PWS patients due to poor outcomes related to an increased risk of rupture of the reduced stomach in the setting of sleeve gastrectomy or gastric bypass procedures, or rupture of the restricted esophagus in the setting of gastric banding procedures with the consequence of life-threatening gastric perforation. Apart from restricted access to food and constant supervision to prevent both life-threatening overeating and morbid obesity, there is currently no treatment for obesity and



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hyperphagia in PWS patients. We recently completed a Phase 2a clinical trial evaluating beloranib's ability to reduce body weight and to improve hyperphagia in PWS patients. In this clinical trial, we observed reductions in body weight, body mass, body fat content and hyperphagia-related behaviors in PWS patients treated with beloranib. We plan to initiate a Phase 3 clinical program, consisting of two Phase 3 clinical trials, of beloranib in PWS patients in 2014 after finalizing the program design based on conversations with the FDA and certain European regulatory authorities.

In January 2013, the FDA granted orphan designation for our application to treat PWS with beloranib. We filed an application to obtain orphan drug designation for beloranib as a treatment for hyperphagia and obesity in PWS in the European Union in early 2014. Orphan drug designation provides for seven years of marketing exclusivity in the United States and ten years of marketing exclusivity in the European Union.

### *Craniopharyngioma-Associated Obesity*

Craniopharyngioma is a rare form of benign brain tumor that occurs near the optic nerve, pituitary gland and hypothalamus. Approximately 30% to 50% of cases of craniopharyngioma are diagnosed in childhood and adolescence. Manifestations of craniopharyngioma include visual disturbances, headaches and impairment to the hypothalamus-pituitary axis affecting hormone secretion. Treatment of these tumors commonly involves radical surgical removal of the tumor mass by endoscopy or craniotomy, followed by radiation treatment, which results in disruption or removal of neighboring structures including the hypothalamus. Depending on the degree of damage to the hypothalamus caused by tumor removal and subsequent radiation, there may be greater variation in hyperphagia and obesity prevalence in craniopharyngioma patients than PWS patients. Post-treatment hypothalamic dysfunction results in hyperphagia in approximately 50% of these patients, resulting in obesity and a worsened quality of life.

Published population studies estimate that the incidence of craniopharyngioma is 0.13 to 0.17 per 100,000 per year, or approximately 400 to 500 cases per year in the United States and 650 to 850 cases per year in the European Union. We believe patients with craniopharyngioma-associated obesity have a longer life expectancy than PWS patients, which contributes to an increased risk of developing obesity-related co-morbid conditions such as type 2 diabetes in such patients.

Currently, there are no pharmacological agents for the treatment of hyperphagia and resultant obesity seen in patients with craniopharyngioma-associated obesity, and bariatric surgery is not frequently employed in this patient population. We believe this is related to perceived risks of surgical interventions in this population including increased risk of post-surgical complications.

We plan to seek orphan drug designation for the treatment of craniopharyngioma-associated obesity in the United States and the European Union, and anticipate initiating a Phase 2a clinical trial, ZAF-221, evaluating the impact of beloranib treatment on body weight, body composition and hyperphagia in patients with craniopharyngioma-associated obesity in the first half of 2014. Depending upon the outcome of our Phase 2a clinical trial, we anticipate that our Phase 3 clinical trial of beloranib as a treatment of craniopharyngioma-associated obesity will evaluate beloranib's impact on weight loss, body composition and hyperphagia.

### *Severe Obesity in the General Population*

Our long-term intention is to pursue clinical development of beloranib or another MetAP2 inhibitor as a treatment for severely obese patients in the general population. We believe this patient population would benefit from MetAP2 inhibitor treatment through the reduction of body weight and through improvement of severity or symptoms of other co-morbid conditions. We believe that MetAP2 inhibitors have the potential to offer this patient population, most of which is not adequately responsive to available therapies, substantial health and quality of life benefits.

The most effective current treatment for severe obesity is bariatric surgery, including procedures such as the Roux-en-Y gastric bypass, adjustable gastric banding, sleeve gastrectomy and biliopancreatic diversion. Bariatric surgery produces dramatic and sustained weight loss, ranging on average from 20% to 35% one year post-



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procedure and reduces overall mortality, but it can result in numerous complications and adverse events including thrombotic events, such as pulmonary embolism, infection, internal bleeding, pulmonary disease and gastrointestinal obstruction, which sometimes requires reoperation during the post-operative period. Longer-term side effects of bariatric surgery, such as poor nutrient absorption, strictures and hernias, have also been observed.

Bariatric surgery eligibility criteria generally identify surgical candidates as those patients with BMIs, greater than 40 kg/m<sup>2</sup>, or those with BMIs over 35 kg/m<sup>2</sup> who also have a significant and uncontrolled co-morbid condition. Based on these criteria, it is estimated conservatively that there will be at least 16 million adults in the United States eligible for bariatric surgery by the time beloranib or another MetAP2 inhibitor could become available commercially. In addition to the BMI and co-morbidity eligibility criteria, patients need to satisfy a number of other criteria in order to have bariatric surgery; a severely obese patient must not have any known endocrine causes of obesity, a drug or alcohol problem, or an uncontrolled psychological condition, and must understand and appreciate the risks of the surgical intervention. According to the American Society for Metabolic & Bariatric Surgery and to HealthGrades, the average cost of bariatric surgery in the United States is approximately \$22,000-\$38,000. As a result of these limiting criteria and the financial commitments required, only a few hundred thousand patients undergo bariatric surgery each year even though over 16 million patients in the United States are eligible for the surgery based on BMI alone.

The pharmaceutical industry has undertaken several waves of activity to discover and develop new drugs for the treatment of obesity. Relative to bariatric surgery, pharmaceutical treatments have produced modest efficacy. In addition, existing pharmacotherapeutics for obesity often have undesirable adverse event profiles.

The following table summarizes information from pivotal trials supporting registration for the current pharmacological treatments for severe obesity and the key limitations of these treatments, and unless specified otherwise in the table below, weight loss data is based on one year or longer treatment with the drug:

<b>Treatment</b>	<b>% Placebo-Adjusted Weight Loss*</b>	<b>Key Limitations**</b>
Phentermine	3.8-4.4% over 6 months	<ul style="list-style-type: none"><li>• Short-term use only</li><li>• Cannot be used in pregnant women</li></ul>
Xenical®/ alli	2-5%	<ul style="list-style-type: none"><li>• Unpleasant gastrointestinal side effects related to dietary fat malabsorption</li></ul>
Qsymia®	6.6% at target dose of 7.5mg/46 mg 8.6% at high dose of 15mg/92mg	<ul style="list-style-type: none"><li>• Known human teratogen – cannot be used in women unless contraception can be assured</li></ul>
Belviq®	3.0-3.3%	<ul style="list-style-type: none"><li>• Should not be taken during pregnancy or by women who are planning to become pregnant</li></ul>

\* Placebo-adjusted weight loss refers to the difference in mean weight loss observed in drug-treated patients and the weight change within the same trial observed in placebo-treated patients. This analysis takes into account, at least in part, the impact of diet and lifestyle interventions employed in drug registration trials.

\*\* Some patients in our clinical trials of beloranib have reported gastrointestinal side effects, such as nausea, diarrhea or vomiting as well as sleep disturbance. In addition, beloranib will likely carry a Category X label and therefore be contraindicated in pregnant women or women looking to become pregnant.

In 2013, we completed a 12-week Phase 2a clinical trial of beloranib administered twice weekly in obese patients. We observed placebo-adjusted weight loss, or weight loss observed beyond that seen in the control arm, of up to 10.3% after 12 weeks of treatment with beloranib. In addition, we observed reductions in levels of low density lipoprotein cholesterol, C-reactive protein and systolic blood pressure. Patients treated with beloranib also reported reduced hunger, as assessed using a visual analog scale, a widely used self-reported measure of hunger and related endpoints. We intend to initiate a Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population. We are also evaluating additional proprietary MetAP2 inhibitors beyond

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beloranib as potential development candidates that would provide increased patient convenience in the form of oral dosing, or an otherwise improved clinical profile. A decision on whether to subsequently advance beloranib into pivotal trials for severe obesity or to leverage the opportunity to advance another MetAP2 inhibitor into early development for severe obesity is anticipated to be made on the basis of results obtained from our planned Phase 3 clinical program of beloranib in PWS patients and discussions with regulatory authorities. Future clinical development may address the impact of beloranib or a related drug on type 2 diabetes and other common co-morbid conditions associated with obesity.

### **Our Strategy**

Our objective is to be a leader in the discovery, development and commercialization of novel therapies to significantly improve the health and well-being of patients affected by obesity. Key elements of our strategy include:

- ***Advance the clinical development of beloranib in subpopulations of obese patients, including those with rare conditions, where obesity is a co-morbidity of an underlying condition.*** Diseases in this category include PWS, hypothalamic damage that is caused by trauma, surgical removal of tumors (including craniopharyngioma), radiation therapy of mid-brain tumors and monogenic loss of function mutations, including leptin deficiency and melanocortin receptor subclass 4 mutations. We believe that rare conditions such as PWS afford us an opportunity to rapidly develop and commercialize beloranib using smaller, more focused and less costly clinical trials, relative to those required to develop beloranib for the broader severe obesity population. Beloranib exerts its weight loss effects using a novel mechanism that does not appear to require fully functioning hypothalamic control pathways. We believe this mechanism is well-suited for patients with obesity that is caused by the failure of hypothalamic food intake control mechanisms, in particular the control of relentless and pathological hunger, or hyperphagia. In 2013, we completed a Phase 2a clinical trial of beloranib as a treatment for obesity in PWS patients, the most common known genetic cause of life-threatening obesity. In this clinical trial, we observed reductions in body weight, body mass, body fat content and hyperphagia-related behaviors in PWS patients treated with beloranib. We expect the full clinical trial report will be available in the second quarter of 2014. We plan to initiate a Phase 3 clinical program, consisting of two Phase 3 clinical trials, of beloranib in PWS patients in 2014, after finalizing the program design based on conversations with the FDA and certain European regulatory authorities. We also plan to initiate a Phase 2a clinical trial of beloranib in patients with craniopharyngioma-associated obesity in the first half of 2014.
- ***Advance the clinical development of MetAP2 inhibitors for the treatment of severely obese patients in the general population, including those who are candidates for bariatric surgery.*** We believe the severely obese patient population would benefit from MetAP2 inhibitor treatment through the reduction of body weight and through improvement of other co-morbid conditions. Bariatric surgery results in significant weight loss, but the financial expense and the potential for complications, adverse events and longer-term side effects limit its overall adoption, with only a few hundred thousand patients in the United States undergoing bariatric surgery each year. Existing pharmacotherapies result in less weight loss than surgical options, and these therapies not only have undesirable side effects, but also have risk of abuse. We recently completed a 12-week Phase 2a clinical trial of beloranib administered twice weekly in obese patients. We observed placebo-adjusted weight loss of up to 10.3% after 12 weeks of treatment with beloranib in addition to reductions in levels of low density lipoprotein cholesterol, C-reactive protein and systolic blood pressure. We intend to initiate a Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population. A decision on whether to subsequently advance beloranib into pivotal trials for severe obesity or to leverage the opportunity to advance another MetAP2 inhibitor into early development for severe obesity is anticipated to be made on the basis of results obtained from our planned Phase 3 clinical program of beloranib in PWS patients and discussions with regulatory authorities.
- ***Leverage the knowledge of our experienced team of drug developers that have deep expertise in the field of obesity, the function of MetAP2 inhibitors and metabolic diseases.*** Our management team has deep expertise in obesity and related metabolic diseases, the function of MetAP2 inhibitors, the strengths

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and weaknesses of current treatments for obesity and the ability to recognize the potential of novel therapies for the treatment of obesity. Our team is complemented by highly experienced external consultants and collaborators in the areas of drug discovery, development and regulatory approval.

- **Maintain flexibility in commercializing and maximizing the value of our development programs.** While we intend to develop and commercialize beloranib for indications such as PWS and other rare conditions causing obesity, we may enter into strategic relationships with biotechnology or pharmaceutical companies to realize the full value of beloranib or our other earlier-stage development programs. For beloranib, we may enter into one or more strategic relationships to access broader geographic markets or additional indications. These relationships could focus on specific patient populations and their caregivers, on regional development, or on distribution and sales of beloranib.
- **Development of other potential product candidates.** We have a second program focused on the delivery of MetAP2 inhibitors with targeted tissue distribution that shows early promise in animal models of abdominal obesity, fatty liver and type 2 diabetes. Our lead MetAP2 inhibitor in this class of molecules is called ZGN-839. We believe that compounds such as ZGN-839 will have utility in the treatment of type 2 diabetes in humans and will further cause improvements in cardiovascular risk factors including low density lipoprotein cholesterol. We plan to advance multiple candidate drugs into early development to establish clinical proof of concept, safety and tolerability of these molecules as a way to leverage our internal know-how in metabolic diseases and the effects of MetAP2 inhibitors. These compounds, typified by ZGN-839, could provide additional short-term value to our company through focused development partnerships and collaborations.

### **Mechanism of Action**

Beloranib is a novel, first-in-class injectable small molecule therapy with a unique mechanism of action that reduces hunger while stimulating the use of stored fat as an energy source. Beloranib is the first new anti-obesity agent with the potential to address two important abnormalities that are present in the obese patient—hunger that is inappropriate relative to the amount of energy stored as fat and dysregulation of fat metabolism, which causes more fat to be made and stored in an obese patient than in a lean person.

Beloranib is a potent inhibitor of MetAP2, an enzyme that modulates the activity of key cellular processes that control metabolism. MetAP2 inhibitors work, at least in part, by directing MetAP2 binding to cellular stress mediators, and, thus, reducing fat synthesis by the liver and fat storage throughout the body. In this manner, MetAP2 inhibition increases metabolism of fats as an energy source. MetAP2 inhibitors also reduce hunger and food intake by novel mechanisms that require further study to be fully understood.

Beloranib was evaluated for its potential for treating obesity following publication of studies in the *Proceedings of the National Academy of Sciences* in 2002 showing anti-obesity efficacy in animals treated with a prototype MetAP2 inhibitor. These studies showed that MetAP2 inhibitor treatment was associated with loss of fat tissue accompanied by an increase in fat oxidation, indicating a redirection of fuel usage toward utilization of stored fats as a source of energy. Reduced food intake also was observed in treated animals, suggesting either direct effects of the agent on central feeding regulation or activation of a feedback loop linking the release and oxidation of stored fat to appetite.

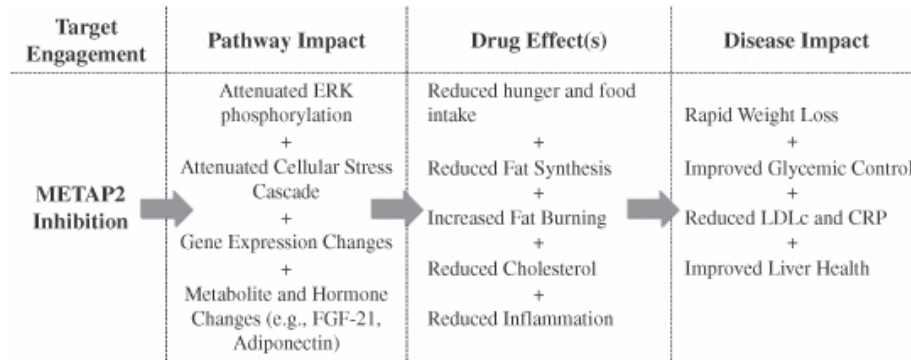
The MetAP2 inhibitor fumagillin, a structural analog of beloranib, was shown in 2004 to induce a novel protein-protein interaction involving MetAP2 and extracellular-signal-regulated kinase 1, or ERK1, a cell stress- and growth factor-stimulated kinase. This complex reduces the activation state of ERK1. A 2005 publication in *Diabetes* showed that animals lacking ERK1 resist both high fat diet-induced obesity and insulin resistance, supporting the hypothesis that attenuation of ERK activity could be an important component of the beneficial metabolic effects of MetAP2 inhibitor treatment. Several hormones well-documented to be involved in energy metabolism are affected by beloranib, including leptin, adiponectin and fibroblast growth factor-21. These hormones are thought to contribute to the weight-reducing effects of beloranib and also are known to be involved

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in control of body weight, fat metabolism and glucose metabolism. This series of mechanistic effects leads to rapid and sustained reduction of excess body weight with beloranib treatment, such as has been observed in animal studies and our clinical trial experience to date.

Our clinical experience to date shows that beloranib treatment is also associated with improvements in cardiovascular disease risk factors such as plasma total cholesterol, high density lipoprotein cholesterol, or HDL, and C-reactive protein, or CRP. Plasma total cholesterol, HDL, CRP, and systolic blood pressure are considered to be the most rigorous systemic biomarkers of cardiovascular disease risk. Our clinical experience to date with beloranib suggests that its use is not associated with an increase in blood pressure or heart rate, which makes it particularly relevant to severely obese patients, in whom a broad spectrum of elevated cardiovascular risk factors often is seen.

An illustration of the MetAP2 inhibitor mechanism of action and therapeutic effects follows:



## Clinical Trials

Beloranib was initially formulated for intravenous administration to facilitate early clinical efforts. Our clinical program has been oriented to first establish whether beloranib would lead to weight loss at tolerated and safe doses, and then to transition to the more convenient subcutaneous injection method of administration for development in our indications of interest, including PWS, craniopharyngioma and severe obesity.

We have completed five clinical trials evaluating beloranib in over 200 patients. Our first three clinical trials, ZAF-001, ZAF-003 and ZAF-101, established a working dose range for beloranib above 0.65 mg and below 3 mg. To further explore the efficacy, safety, tolerability and impact of beloranib on severe obesity, we conducted ZAF-201, a 12-week clinical trial of beloranib administered twice weekly to 124 obese patients at doses of 0.6 mg, 1.2 mg, and 2.4 mg. This placebo-controlled, double-blinded trial, established that the efficacy of beloranib continued beyond four weeks and was associated with sustained impact on key biomarkers of effect.

These clinical trials set the stage for continued evaluation of beloranib, by subcutaneous administration, in PWS patients. ZAF-211 was a placebo-controlled, double-blinded trial evaluating safety and tolerability as well as the effects of 1.2 mg or 1.8 mg doses of beloranib in patients with PWS on body weight, body composition and hyperphagia-related behaviors.

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The table below summarizes the structure of and key findings from these five clinical trials of beloranib.

<b>Trial Number</b>	<b>Brief Description</b>	<b>Treatment Duration</b>	<b>BMI Range of Patients (kg/m<sup>2</sup>)</b>	<b>Observations</b>
ZAF-001 <i>Phase 1b</i>	<ul style="list-style-type: none"> <li>• Randomized, double-blind, placebo-controlled trial</li> <li>• Escalating doses of 0.1 mg/m<sup>2</sup>, 0.3 mg/m<sup>2</sup>, and 0.9 mg/m<sup>2</sup>, or approx. 0.2 mg, 0.6 mg, and 2 mg</li> <li>• 1-hour intravenous infusion twice weekly</li> </ul>	4 weeks	32-45	<ul style="list-style-type: none"> <li>• Dose dependent weight reductions with 0.9 mg/m<sup>2</sup> twice weekly resulting in -3.6 kg weight loss versus -1.2 kg change with placebo over 4 weeks</li> <li>• Metabolic benefits (C-reactive protein and metabolic hormones) observed in dose dependent fashion</li> <li>• Safe and well tolerated at all dose levels</li> </ul>
ZAF-003 <i>Phase 1b</i>	<ul style="list-style-type: none"> <li>• Randomized, double-blind, placebo-controlled trial</li> <li>• Static dosing scheme of 3.0 mg, 6.0 mg, and 2.5 mg</li> <li>• 1-hour intravenous infusion               <ul style="list-style-type: none"> <li>• 3.0 mg and 6.0 mg doses given twice weekly for 4 weeks</li> <li>• 2.5 mg dose given twice weekly for the first week and once weekly for the subsequent 6 weeks.</li> </ul> </li> </ul>	4 weeks or 7 weeks	30-50	<ul style="list-style-type: none"> <li>• Dose dependent weight reductions with 6.0 mg dose resulting in -6.7 kg weight loss, 3.0 mg in -4.7 kg, and placebo in -0.3 kg over 4 weeks</li> <li>• Once weekly 2.5 mg dose resulted in weight loss of -3.1 kg over 7 weeks and with greater variability</li> <li>• 6.0 mg not very well tolerated with gastrointestinal side effects and sleep disturbance emerging as dose limiting adverse effects; Doses of 3.0 mg or lower were well tolerated and effective</li> <li>• Once-weekly regimen was less effective than bi-weekly administration</li> </ul>
ZAF-101 <i>Phase 1b</i>	<ul style="list-style-type: none"> <li>• Randomized, double-blind, placebo-controlled trial</li> <li>• 1.0 mg, 2.0 mg, and 4.0 mg were evaluated</li> <li>• Subcutaneous injection twice weekly</li> </ul>	4 weeks	30-45	<ul style="list-style-type: none"> <li>• Significant weight reduction with all doses; 4.0 mg dose resulting in -6.1 kg, 2.0 mg in -4.2 kg, 1.0 mg in -4.3 kg, and placebo in -1.2 kg</li> <li>• Comparable metabolic benefits observed as in prior trials, including body composition improvements; sense of hunger reduced with all doses</li> <li>• 4.0 mg not as well tolerated with similar adverse event profiles as with 6.0 mg intravenous dose in ZAF-003 – mainly gastrointestinal side effects and sleep disturbances; injection site adverse events unremarkable</li> </ul>
ZAF-201 <i>Phase 2a</i>	<ul style="list-style-type: none"> <li>• Randomized, placebo controlled, double-blinded, parallel design trial</li> <li>• Fixed beloranib doses including 0.3 mg, 0.6 mg, 1.2 mg, 2.4 mg, and 3.2 mg or placebo</li> <li>• Subcutaneous injections twice weekly</li> </ul>	12 weeks	30-50	<ul style="list-style-type: none"> <li>• 0.3 mg not effective, 3.2 mg not well tolerated; both doses eliminated after first 2-4 weeks of dosing (pre-defined)</li> <li>• Progressive and dose dependent weight reduction; -10.9 kg in the 2.4 mg group, -6.9 kg in the 1.2 mg group, -5.5 kg in the 0.6 mg group, versus -0.4 kg in placebo</li> <li>• Comparable metabolic and body composition benefits observed as with prior studies</li> <li>• Most adverse events, including sleep disturbances, mild-moderate and transient</li> </ul>

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ZAF-211 <i>Phase 2a</i>	<ul style="list-style-type: none"><li>• Randomized, double-blind, parallel design trial</li><li>• 1.2 mg and 1.8 mg doses of beloranib or placebo in patients with Prader-Willi Syndrome</li><li>• Subcutaneous injections twice weekly</li></ul>	4 weeks	26-44	<ul style="list-style-type: none"><li>• Trend toward reduction in body weight measured by scale weight; -1.27% in beloranib-treated patients (pooled analysis of 1.2 and 1.8 mg treatment groups) versus +0.34% change in placebo-treated patients</li><li>• Reduction in body mass assessed by dual-energy x-ray absorptiometry (DEXA); -2.1% in beloranib-treated patients versus +2.0% change in placebo-treated patients</li><li>• Reduction in total fat mass assessed by DEXA; -2.9% in beloranib-treated patients versus +3.6% change in placebo-treated patients</li><li>• Reduction in hyperphagia related behaviors (at 1.8 mg dose level only).</li></ul>
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Across all our clinical trials, beloranib has been well-tolerated at doses we would expect to explore in the future. There have been no serious adverse events, or SAEs, attributed to beloranib in our clinical trials. The main adverse events, or AEs, including those leading to drop-outs, in patients dosed with beloranib have been sleep disturbances, principally manifested as delayed onset of sleep, nausea and vomiting. For certain of our clinical trials, we performed statistical analysis of our results and report the p-value, which is a statistical calculation that relates to the probability that a difference between groups happened by chance, with a p-value of less than 0.05 (i.e., less than 5% probability that the difference happened by chance) generally being used as the threshold to indicate statistical significance. We expect that the FDA will perform its own independent statistical analyses to determine if our data support regulatory approval. Each of our clinical trials is discussed in more detail below.

### *Phase 1b Clinical Trials*

#### **ZAF-001—A Randomized, Double-Blind, Placebo-Controlled Multiple Dose Study, to Assess Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ZGN-433 (Beloranib for Intravenous Infusion) in Obese Volunteers**

ZAF-001 was a four-week double-blind, placebo controlled, dose escalation and multiple dose trial conducted in Australia. The primary clinical endpoints of this clinical trial were safety, tolerability, pharmacokinetics and pharmacodynamics of beloranib administered by intravenous administration. 31 Caucasian female patients, with an average age of 52.2 years and BMI range of 32-45 kg/m<sup>2</sup>, were enrolled in this clinical trial. 22 patients received beloranib and nine patients received placebo. The patients were divided into three different cohorts, with each cohort receiving 0.10 mg/m<sup>2</sup>, 0.30 mg/m<sup>2</sup>, or 0.90 mg/m<sup>2</sup> of beloranib or placebo via intravenous infusion twice weekly for four weeks. The primary objectives of this clinical trial were to (i) evaluate the safety and tolerability of beloranib in obese patients and (ii) determine the plasma pharmacokinetics and pharmacodynamics of beloranib in obese patients. A secondary objective was to obtain information on weight loss in obese patients exposed to beloranib for eight intravenous doses over a one-month period. A total of 26 of the 31 enrolled patients completed this clinical trial as planned, receiving all 8 infusions of study drug. Three placebo patients and two beloranib-treated patients withdrew from this clinical trial because of loss of venous access and other reasons unrelated to drug treatment.

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The key results of this clinical trial are summarized for the Per Protocol population, patients completing the full dosing period and receiving a minimum of six doses, as follows:

### 4-week Phase 1b Proof of Concept Clinical Trial in Obese Patients (ZAF-001)

<u>Trial Arm</u>	<u>Number of Patients Per Protocol</u>	<u>Baseline Body Weight (kg)</u>	<u>Average Weight Change (kg)</u>	<u>p-value*</u>
Placebo	6	96.0	-1.2	—
Beloranib 0.1 mg/m <sup>2</sup>	6	105.3	-0.9	—
Beloranib 0.3 mg/m <sup>2</sup>	6	100.3	-1.3	—
Beloranib 0.9 mg/m <sup>2</sup>	8	104.2	-3.6	—

\* statistical analysis was not performed in this proof of concept trial

- Post hoc analyses suggested that beloranib had favorable effects on other parameters, including body fat content, C-reactive protein, low density lipoprotein cholesterol and hunger.

There were no drug-related SAEs or treatment emergent adverse events, or TEAEs. Headaches and gastrointestinal symptoms were the most common TEAEs in all groups including placebo and tended to be mild in intensity and transient. Contusions or bruising which occurred at infusion sites, often due to difficulty in IV access, were reported. There were no clinically significant changes reported as TEAEs in hematology, serum chemistry or urinalysis values for any of the patients in any of the dose groups. The objectives of this clinical trial were met. Weight loss was a secondary clinical endpoint and was not subjected to statistical analysis.

### **ZAF-003—Phase 1b Trial of Beloranib, a Novel Methionine Aminopeptidase 2 (MetAP-2) Inhibitor for Treatment of Extreme Obesity: Randomized, Double-Blind, Placebo-Controlled, Escalating Doses in Female Volunteers**

ZAF-003 was a double-blind, placebo controlled, dose escalation and multiple dose trial conducted in Australia. A static dosing scheme of 3.0 mg, 6.0 mg, and 2.5 mg was evaluated and all doses were administered via 1-hour intravenous infusion, with 3.0 mg and 6.0 mg doses given twice weekly for four weeks, and the 2.5 mg dose given twice weekly for the first week and once weekly for the subsequent six weeks for total of seven weeks of treatment. Patients who qualified after the screening round were randomized 2:1 to treatment with beloranib or placebo. 25 obese female patients were enrolled, and 22 patients completed this clinical trial. Three patients withdrew from this clinical trial, two from the 6.0 mg treatment group, due to tolerability limitations and one from the 2.5 mg treatment group due to an adverse event deemed not to be related to study drug. 92% of the patients were Caucasian, 4% of the patients were Asian and 4% of the patients were Pacific Islanders. The average ages were between 44.0 and 51.3 years for the various treatment groups. The primary objective of this clinical trial was to demonstrate safe doses of intravenous infusion of beloranib for reduction of body weight in female obese patients with baseline BMIs ranging from 30 to 50 kg/m<sup>2</sup>. The secondary objectives of this clinical trial were to (i) confirm the safety profile of beloranib in obese female patients receiving incrementally larger fixed doses than the dose regimen previously tested in ZAF-001, (ii) evaluate the tolerance, weight loss and ease of administration for continuing a safe dose of beloranib on a weekly schedule, (iii) correlate higher dose levels of beloranib with measures of reduction in body weight and hunger, (iv) confirm the pharmacokinetic profile of beloranib, and (v) correlate exposure of beloranib with changes in biomarkers for fasting plasma lipids, lipid metabolism, fasting insulin and thyroid function.

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The key results of this clinical trial are summarized for the Per Protocol population, patients completing the full dosing period and receiving a minimum of six doses, as follows:

### 4-week Phase 1b Proof of Concept Clinical Trial in Obese Patients (ZAF-003)

<u>Trial Arm</u>	<u>Number of Patients Per Protocol</u>	<u>Baseline Body Weight (kg)</u>	<u>Average Weight Change (kg)</u>	<u>p-value*</u>
Placebo	8	104.6	-0.1	—
Beloranib 3.0 mg twice weekly	6	102.3	-4.7	—
Beloranib 6.0 mg twice weekly	3	105.5	-6.7	—
Beloranib 2.5 mg once weekly	5	94.0	-2.7	—

\* statistical analysis was not performed in this proof of concept trial

- Post hoc analyses suggested that beloranib had favorable effects on other parameters, including body fat content, C-reactive protein, low density lipoprotein cholesterol and hunger.

The primary and secondary objectives of this clinical trial were met, showing the maximally tolerated dose of 3.0 mg of beloranib administered by intravenous infusion was identified, weight loss was uniformly observed at both 3.0 mg and 6.0 mg dose levels of beloranib, and a visual analog scale of hunger revealed reduction in hunger at both doses. Further, a once-weekly regimen was evaluated with 2.5 mg of beloranib, which was well-tolerated and showed limited evidence of weight loss efficacy or reduction in hunger despite being well-tolerated.

### ZAF-101- ZGN-440 (Beloranib for Subcutaneous Injection), A Novel Methionine Aminopeptidase 2 Inhibitor for Treatment of Obesity: A Randomized Double-Blind Placebo Controlled Dose Escalation Phase 1b Trial to Evaluate Safety, Pharmacokinetics, Pharmacodynamics and Initial Weight Loss

ZAF-101 was a four-week, multi-dose trial using beloranib formulated for subcutaneous, or SC, injection in obese, otherwise healthy females, conducted in Australia. This clinical trial was a double-blind, placebo controlled, dose escalation and multiple dose study. Doses of 1.0 mg, 2.0 mg, and 4.0 mg of beloranib were evaluated and all doses were administered by SC injection twice weekly for four weeks. Patients who qualified after the screening were randomized 1:1:1:1 to treatment with the three dose levels of beloranib or placebo. 25 female Caucasian patients were enrolled. Four patients withdrew from this clinical trial, three from the 4.0 mg treatment group and one from the 2.0 mg treatment group due to sleep disturbance. The average ages were 46.0 to 49.9 years for the various treatment groups and the BMI range of the patients was 30-45 kg/m<sup>2</sup>. This clinical trial was designed to evaluate the safety and tolerability of beloranib administered SC in obese female patients. Secondary objectives of this clinical trial were to assess weight loss and responses in metabolic biomarkers over a dose range of beloranib in obese female patients and to compare weight loss due to beloranib administered SC to that previously observed by beloranib administered intravenously.

The key results of this clinical trial are summarized for the Per Protocol population, patients completing the four-week dosing period and receiving a minimum of six doses, as follows:

### 4-week Phase 1b Proof of Concept Clinical Trial in Obese Patients (ZAF-101)

<u>Trial Arm</u>	<u>Number of Patients Per Protocol</u>	<u>Baseline Body Weight (kg)</u>	<u>Average Weight Change (kg)</u>	<u>p-value</u>
Placebo	6	97.3	-1.2	—
Beloranib 1.0 mg	6	99.1	-4.3	<0.001
Beloranib 2.0 mg	5	92.7	-4.2	<0.001
Beloranib 4.0 mg	4	93.9	-6.1	<0.001



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There were no clinically significant changes in laboratory parameters, electrocardiograms, or vital signs with any of the doses. There were no deaths or severe AEs reported in this clinical trial. Aside from mild and transient injection site reactions, which were observed across all treatment groups, including placebo, SC administration of the drug appeared to be locally well-tolerated. However, the highest dose, or 4.0 mg of beloranib, appeared to be less well-tolerated systemically and led to more frequent moderate intensity TEAEs and premature trial withdrawals, mainly due to gastrointestinal events and sleep disturbance. Sleep disturbance AEs were reported by 100% of subjects in the 2.0 mg group (6 events), 85.7% of subjects in the 4.0 mg group (6 events), 83.3% of subjects in the 1.0 mg treatment group (5 events) and 16.7% of subjects in the placebo treatment group (1 event). All events of sleep disturbance were deemed to be probably related to study drug. Abnormal dreams, mostly vivid dreams, were the other frequently reported sleep abnormalities reported as TEAEs reported by 83.3% of subjects in the 2.0 mg dose group, 85.7% in the 4.0 mg dose group and 66.7% in the 1.0 mg dose group. No subjects reported abnormal dreams in the placebo group. The majority of sleep disorders were of mild severity—83.3% in the 2.0 mg dose group, 33.3% in the 4.0 mg dose group, 100% in the 1.0 mg dose group; as were the majority of abnormal dreams—83.3% in the 2.0 mg dose group, 85.7% in the 4.0 mg dose group, and 66.7% in the 1.0 mg dose group. All remaining events were moderate in severity. A total of four subjects including one subject in the 2.0 mg dose group and three subjects from the 4.0 mg dose group withdrew from the trial due to sleep disturbance. The increased incidence of early trial withdrawal due to sleep disturbance in the 4.0 mg treatment group suggested that this dose was less well tolerated. Gastrointestinal disorders were frequently reported across all dose groups. The greatest percentage of subjects to report gastrointestinal adverse events, such as diarrhea and nausea, were in the placebo group, 50.0% (3 events in 3 subjects) and 33.3% (2 events in 2 subjects), respectively. Occurrence of diarrhea in beloranib-treated subjects ranged between 16.7% (1 event in 1 subject) for the 2.0 mg dose group, and 42.9% (3 events in 3 subjects) in the 4.0 mg dose group. Occurrence of nausea in beloranib-treated subjects ranged from 14.3% (1 event in 1 subject) for the 4.0 mg dose group, and 16.7% (1 event in 1 subject) in both the 1.0 and 2.0 mg dose groups.

### *Phase 2a Clinical Trials*

#### **ZAF-201—Randomized, Double-Blind, Placebo-Controlled, Dose Ranging Phase 2 Trial of Beloranib (ZGN-440 for Subcutaneous Injection), A Novel Methionine Aminopeptidase 2 Inhibitor, in Obese Subjects to Evaluate Weight Reduction, Safety, and Pharmacokinetics Over 12 Weeks**

ZAF-201 was a 12-week Phase 2a proof-of-concept clinical trial in 160 obese patients, of whom 122 were dosed with beloranib, across eight participating trial sites in Australia. 93.8% of patients were female, 97.5% were Caucasian, the average age was 48.4 years and patients had a BMI range of 30-54 kg/m<sup>2</sup>. Patients were excluded from this clinical trial if they had been involved recently in another weight loss trial, or if they had clinically significant liver, renal, pulmonary, cardiovascular, oncologic, gastrointestinal disease, or severe mental illness. This clinical trial was designed to evaluate weight loss and responses in metabolic biomarkers over a dose range of beloranib and to assess safety and tolerability of beloranib over 12 weeks in obese patients. This was a randomized, placebo controlled, double-blinded, parallel design trial to evaluate a range of fixed beloranib doses, including 0.3 mg, 0.6 mg, 1.2 mg, 2.4 mg and 3.2 mg, in comparison to placebo. All doses were administered as SC injections twice weekly for 12 weeks.

Trial endpoints included safety and tolerability, weight loss, body composition by bio-impedance, pharmacokinetic, or PK, and pharmacodynamic assessment. As stipulated in the protocol, our Safety Review Committee for this clinical trial, or SRC, reviewed interim safety and PK results after 36 patients from the initial part of this clinical trial completed at least 2 weeks of treatment. Laboratory, electrocardiogram, and vital sign reviews were deemed to be unremarkable and lacking any significant safety concerns. The SRC recommended to eliminate the lowest and highest active dose groups, 0.3 mg and 3.2 mg, thus leaving the doses of 0.6 mg, 1.2 mg, 2.4 mg or placebo to be studied in the remainder of this clinical trial. This was based on the conclusion that the weight loss for the 0.3 mg dose was not clinically meaningful and the 3.2 mg dose was not well-tolerated. The most common AE leading to early termination at the 2.4 mg and 3.2 mg dose levels was sleep disturbance.

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As severely obese patients are at an increased risk for cardiovascular disease, we measured systemic biomarkers of cardiovascular disease risk, including low density lipoprotein cholesterol, HDL, CRP, triglycerides and blood pressure in trial participants, to determine beloranib's impact on such biomarkers. The results of these biomarker measurements in this trial, as summarized below, suggest that beloranib treatment does not increase the risk of cardiovascular disease and may be associated with reduced cardiovascular disease risk. While we plan to include biomarkers of cardiovascular disease risk as an endpoint for our planned Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population, this trial will not be designed to establish the impact of beloranib treatment on cardiovascular disease risks.

The key results of this trial are summarized for the Per Protocol population, patients completing the 12-week dosing period and receiving a minimum of 16 of 24 doses, as follows:

### 12-week Phase 2a Proof of Concept Clinical Trial in Obese Patients (ZAF-201)

Trial Arm	Number of Patients Per Protocol	Baseline Body Weight (kg)	Mean Weight Change (kg)	Percent Placebo-Adjusted Weight Change	p-value
Placebo	36	102.3	-0.4	—	—
Beloranib 0.6 mg	34	102.6	-5.5	-5.0	<0.0001
Beloranib 1.2 mg	31	102.6	-6.9	-6.4	<0.0001
Beloranib 2.4 mg	15	102.2	-10.9	-10.3	<0.0001

- Levels of the cardiovascular disease risk marker C-reactive protein were reduced by an average of 2.5, 2.3 and 1.9 µg/ml, or 23%, 22% and 37%, respectively, for patients treated with beloranib at 0.6 mg, 1.2 mg and 2.4 mg, respectively, compared to an average increase of 1.0 µg/ml for patients dosed with placebo (p<0.0001).
- Levels of low density lipoprotein cholesterol, or LDL-c, were reduced by an average of 0.3, 0.5 and 1.0 mmol/l, or 9.4%, 14.5% and 29.7%, respectively, for patients treated with beloranib at 0.6 mg, 1.2 mg and 2.4 mg, respectively, compared to an average reduction of 0.3 mmol/l for patients dosed with placebo (p<0.001 for patients treated with 2.4 mg beloranib).
- Levels of high density lipoprotein cholesterol, or HDL-c, were increased by an average of 0.1, 0.1 and 0.2 mmol/l, or 7.6%, 11.6% and 14.6%, respectively, for patients treated with beloranib at 0.6 mg, 1.2 mg and 2.4 mg, respectively, compared to no change for patients dosed with placebo (p<0.05 for patients treated with 1.2 mg and 2.4 mg beloranib).
- Levels of triglycerides were reduced by an average of 0.2, 0.3 and 0.4 mmol/l, or 8.8%, 9.0% and 20.3%, respectively, for patients treated with beloranib at 0.6 mg, 1.2 mg and 2.4 mg, respectively, compared to a reduction of 0.3 mmol/l for patients dosed with placebo (p<0.05 for patients treated with 1.2 mg and 2.4 mg beloranib).
- Systolic blood pressure was reduced by an average of 6.3 mmHg, 6.3 mmHg and 13.6 mmHg for patients treated with beloranib at 0.6 mg, 1.2 mg and 2.4 mg, respectively, compared to an average of 1.4 mmHg reduction for patients dosed with placebo (p<0.05 for 1.2 mg and 2.4 mg doses). Trends toward reduction in diastolic blood pressure also were observed, although these changes did not reach statistical significance.
- Sense of hunger was reduced by an average of 1.5 cm, 2.2 cm and 3.3 cm (out of a maximum number of 10 cm using a standardized visual analog scale asking how hungry the participant had been over the prior trial days) and compared to an average reduction of 0.1 cm in placebo, respectively (p<0.05 for all doses). Baseline values were, on average, 5.0 cm, 5.3 cm, 5.8 cm and 6.4 cm for placebo, for doses of 0.6 mg, 1.2 mg and 2.4 mg of beloranib, respectively.
- Post hoc analyses suggest that beloranib also may have favorable effects on body fat content.

While results from this clinical trial showed that beloranib doses ranging from 0.6 mg to 2.4 mg administered by SC injection resulted in dose-related weight loss, the highest dose, 2.4 mg, was associated with the most significant and rapid onset of weight loss whereas the lower doses, 0.6 mg and 1.2 mg, tended to result

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in slower initiation of weight reduction. However, the highest dose, 2.4 mg, of beloranib appeared to be less well-tolerated systemically and led to more frequent severe intensity TEAEs. 21 patients treated with 2.4 mg beloranib prematurely withdrew from the trial, mainly due to sleep disturbance reflective of increased sleep latency, the time patients reported taking to fall asleep at night. There were no deaths or any SAEs deemed to be possibly, probably, or definitely related to beloranib, although there were two serious thrombotic adverse events which, while not attributed to beloranib treatment, may point to the utility of assessment of prior history of thrombotic events in patients enrolled in subsequent trials and added vigilance for AEs related to blood clotting during future clinical trials. The most commonly reported TEAEs were gastrointestinal disorders, mainly nausea, diarrhea, or vomiting, nervous system disorders, mainly dizziness, and psychiatric disorders, mainly insomnia, sleep disorder, or abnormal dreams. TEAEs were generally mild in severity and transient. Other frequently reported TEAEs were headaches and injection site bruising/itching, although the incidences were comparable to placebo and not observed to be dose-related. Laboratory assessments, vital signs and electrocardiograms revealed no unexplained abnormalities or clinically significant trends. The primary objectives of this clinical trial were met, including demonstration of continued weight loss beyond the four-week trial duration evaluated in prior trials, demonstration of the tolerability profile at effective doses, and demonstration of reductions in key cardiometabolic risk parameters and hunger as well as improved body composition (reduced waist circumference and fat mass) as assessed by bioelectrical impedance.

### **ZAF-211—Randomized, Double-Blind, Placebo Controlled, Parallel Dose Ranging Phase 2a Trial of ZGN-440 (for Subcutaneous Injection), A Novel Methionine Aminopeptidase 2 Inhibitor, in Over-weight and Obese Subjects with Prader-Willi Syndrome to Evaluate Weight Reduction, Food-related Behavior, Safety, and Pharmacokinetics Over 4 Weeks Followed by Optional 4-Week Open-Label Extension**

Our Phase 2a clinical trial of beloranib as a potential treatment of PWS was designed as a randomized, double-blind, and parallel comparison of each of 1.2 mg and 1.8 mg dose levels of beloranib, and placebo. 17 adult PWS patients living in closely-controlled PWS-specific group homes were randomized to one of the three dosing arms, with 6, 5, and 6 patients being randomized to placebo, 1.2 mg beloranib and 1.8 mg beloranib treatment. During the course of the trial, including a two week placebo run-in phase, daily calorie allowances were increased in all patients by 50 percent to drive modest weight gain and simulate the greater access to food experienced in the general PWS population living in family home situations. All patients completed randomized treatment. The primary objectives of this clinical trial were to (i) assess the safety and tolerability of beloranib administered twice weekly SC in PWS patients, (ii) assess body weight change, changes in body mass and fat content by DEXA, scan analysis, and responses in metabolic biomarkers over a dose range of beloranib, and (iii) evaluate changes in quality of life, PWS-specific hyperphagia-related behaviors and/or psychiatric status. The secondary objective of this clinical trial is to evaluate pharmacodynamics and apparent bioavailability over a dose range of beloranib. The randomized treatment period was followed by an optional open-label extension offering patients the opportunity to continue for an additional four weeks of treatment with 1.8 mg beloranib. The results of the open-label extension, which includes all 17 patients initially included in the randomized treatment phase, are expected to be available in early 2014.

The key results of this clinical trial are summarized as follows. Both doses of beloranib have been combined as shown below, as a component of the pre-specified statistical analysis:

#### **Four-Week Phase 2a Proof of Concept Clinical Trial in Patients with Prader-Willi Syndrome (ZAF-211)**

<b>Endpoint</b>	<b>Placebo Baseline (N=6)</b>	<b>Placebo Change (%)</b>	<b>Beloranib Baseline (N=11)</b>	<b>Beloranib Change (%)</b>	<b>p value (Beloranib vs. Placebo)</b>
Body weight (kg) (Scale weight)	70.1	0.34	72.0	-1.3	0.17*
Body mass (kg) (DEXA)	69.7	2.0	72.1	-2.1	0.002
Fat mass (kg) (DEXA)	31.1	3.6	34.6	-2.9	0.013

\* not statistically significant by ANCOVA, or analysis of covariance, a pre-specified statistical analysis, used to assess changes in all key endpoints. ANCOVA is a standard statistical test that takes into account the baseline measurements for each subject.

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- Levels of high density lipoprotein cholesterol were increased by an average of 26% in beloranib-treated patients, compared to an average increase of 1% in patients dosed with placebo ( $p=0.005$ ).
- Levels of low density lipoprotein cholesterol were reduced by an average of 27% in beloranib-treated patients, compared to an average increase of 3% in patients dosed with placebo ( $p=0.005$ ).
- Hyperphagia related behaviors typical of PWS patients were reduced by an average of 52.4% by treatment with 1.8 mg beloranib, compared to an average increase of 40.5% in patients dosed with placebo and an average increase of 1.8% in patients treated with 1.2 mg beloranib. The change in behavior was statistically significant from baseline for the patients treated with 1.8 mg beloranib (not statistically significant by ANCOVA;  $p=0.025$  by post hoc paired t-test).

There were no clinically significant changes in laboratory parameters, electrocardiograms and vital signs with any of the doses. There were no deaths, SAEs, or severe AEs reported in this clinical trial. Aside from mild and transient injection site reactions, which were observed across all treatment groups, including placebo, SC administration of the drug appeared to be locally well-tolerated.

Unlike patients with severe obesity in the general population, PWS patients are missing the function of multiple genes. In order to determine if the underlying mechanistic pathway of beloranib was engaged in PWS patients, we measured levels of low density lipoprotein cholesterol and fat mass. MetAP2 inhibitors, such as beloranib, work, at least in part, by directing MetAP2 binding to cellular stress mediators, and, thus, reducing fat synthesis by the liver and fat storage throughout the body, leading to a reduction in cholesterol, evidenced by reduced levels of low density lipoprotein cholesterol and reduced fat mass. In this clinical trial, PWS patients treated with beloranib had both reduced levels of low density lipoprotein cholesterol and fat mass, suggesting that PWS patients respond to beloranib treatment in a similar manner as severely obese patients that are not missing the function of multiple genes. Likewise, while exploratory, salutary effects on behaviors were observed, which reached clinical significance for the 1.8 mg beloranib treatment arm. These behavioral changes include a range of aspects of the PWS phenotype recorded by the caregiver-administered hyperphagia-related behavior questionnaire, an instrument that measures the frequency and severity of behavioral issues typical of PWS patients that we are currently validating with the FDA for support of our pivotal trials. Together these results, we believe, are strongly supportive of additional studies of beloranib in the PWS patient population.

### ***Clinical Trial Summary***

Our clinical trials suggest that administration of beloranib by intravenous infusion twice weekly for four weeks, or eight doses, at dose levels of up to 3.0 mg was safe and well-tolerated. The incidence and severity of AEs was similar across all dose groups in this range. While these clinical trials were of short duration and designed to demonstrate safety and tolerability, significant decreases in body weight and large decreases in sense of hunger were observed in beloranib-treated patients when compared to the placebo group. Additional clinical trials of longer-term treatment with beloranib designed to demonstrate efficacy are required before we can submit an NDA for beloranib as a treatment for any indication that we are pursuing. In our planned Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population and our planned Phase 3 clinical program of beloranib as a treatment for PWS patients, patients will be treated with beloranib for a substantially longer period of time than as treated in our earlier clinical trials. A SC formulation of beloranib for human use was developed and completed human testing in a Phase 1b clinical trial, which showed that doses ranging from 1.0 mg to 4.0 mg administered by SC injection resulted in statistically significant dose-related weight loss. While the highest dose of 4.0 mg was associated with the most significant weight loss, it appeared to be less well-tolerated systemically and led to more frequent moderate intensity TEAEs and premature trial withdrawals, mainly due to gastrointestinal events and sleep disturbance. There have been no deaths or drug-related SAEs. Laboratory safety measures, vital signs and electrocardiograms have been unremarkable in all completed clinical trials for all doses tested. A 12-week Phase 2a clinical trial, ZAF-201, using subcutaneously administered doses of 0.6 mg, 1.2 mg and 2.4 mg of beloranib has confirmed these earlier observations, and we have observed continued weight loss with maintenance of the key favorable drug effects on body composition, hunger and C-reactive protein levels. A further salutary effect on blood pressure has been identified, strengthening our view that beloranib will have a favorable impact on cardiovascular disease risk.

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ZAF-211 was our first clinical trial in PWS patients using doses of 1.2 mg and 1.8 mg beloranib administered by subcutaneous injection twice weekly for four weeks. This initial clinical trial has generated promising results, with beloranib-treated patients showing reductions in body mass and body fat content, along with improvements in hyperphagia-related behavior. Taken together with the results of our previous clinical trials, we believe there is a very compelling basis for continued development of beloranib for the treatment for rare conditions such as PWS and craniopharyngioma, where obesity is a co-morbidity of an underlying condition, and severe obesity in the general population.

### *Nest Steps*

#### *Planned Pivotal Phase 3 Program of Beloranib for the Treatment of PWS Patients*

We plan to continue the development of beloranib, with an initial focus on the treatment of PWS patients. The proposed design of our pivotal Phase 3 clinical program is based on:

- The results we observed in our Phase 2a clinical trial of beloranib for the treatment of PWS patients; and
- Discussions with the FDA's Division of Metabolism and Endocrinology Products and with representative country organizations in Europe from the Netherlands, Sweden, and France regarding the requirements for our Phase 3 clinical program.

In light of the guidance we have received from the FDA and European health authorities in February and April 2014, respectively, we do not intend to seek a Special Protocol Assessment, which is a declaration from the FDA that the protocols for our planned Phase 3 clinical program are acceptable for regulatory approval. However, prior to the initiation of our planned Phase 3 clinical program, we intend to engage in additional discussions with the FDA and the European health authorities to determine if our proposed Phase 3 clinical trial protocols, including trial designs and selected endpoints, would be sufficient to support an NDA submission to the FDA and a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, seeking approval of beloranib for the treatment of PWS in both the United States and the European Union. Despite the guidance received from these authorities and the guidance that will be received from these authorities, both the FDA and the European health agencies can change their positions on the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete additional clinical trials or impose stricter approval conditions than we currently expect.

Based on discussions with the regulatory authorities to date, we currently expect our pivotal Phase 3 clinical program to consist of two Phase 3 clinical trials, one in the United States and the other in the European Union, to evaluate the efficacy, safety and tolerability of 1.8 mg and 2.4 mg beloranib versus placebo over six months of randomized, double-blinded treatment of patients with PWS. We propose that both trials include open label extensions to allow for further evaluation of beloranib's safety following an additional six months of treatment. We plan on enrolling a total of approximately 240 total patients in the two trials, and plan to conduct these trials in outpatient settings, both in family homes and in group homes that specialize in the care of patients with developmental disabilities.

#### *Planned Pivotal Phase 3 Clinical Program Endpoints*

Based on our communications with the FDA and European health authorities, our proposed Phase 3 clinical trial protocols currently provide that in order to support an NDA submission to the FDA and an MAA submission to the EMA, we must demonstrate in two Phase 3 clinical trials a statistically significant and clinically meaningful improvement in either (i) total body fat mass or (ii) hyperphagia-related behaviors in patients treated with beloranib compared to patients receiving placebo. We expect that total body fat mass, a key physical derangement of obesity that is increased substantially and pathologically in PWS patients, will be defined as a percentage change in body fat content as measured using dual emission X-ray absorptiometry, or DEXA, from

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baseline to six months with beloranib treatment compared to a change from baseline to six months in patients treated with placebo. We expect that hyperphagia-related behaviors will be measured by the PWS-HQ that was used in our Phase 2a clinical trial of beloranib in PWS patients. The PWS-HQ is undergoing validation under guidance of the FDA Study Endpoints and Labeling Development staff, which we expect to be completed during the course of our Phase 3 program but prior to regulatory filing. If we fail to validate the PWS-HQ in time for it to be an effective tool to evaluate data from our Phase 3 clinical trial, our Phase 3 program and, in turn, our regulatory filing may be delayed until we validate the tool or develop a new one.

We expect to include change in total body mass, measured by DEXA, and change in body weight measured by scale as secondary endpoints in both of our pivotal Phase 3 clinical trials. In addition, we expect to include other secondary endpoints such as the evaluation of changes in key biomarkers of beloranib response, including low density lipoprotein cholesterol, high density lipoprotein cholesterol, C-reactive protein concentrations, number of active skin lesions related to skin-picking behavior, and quality of life.

In addition to efficacy endpoints, our Phase 3 clinical trial protocols assume that in order to support an NDA submission to the FDA and an MAA submission to the EMA, we must demonstrate the safety and tolerability of beloranib over one year of dosing.

### *Planned Pivotal Phase 3 Clinical Program Trials' Design*

We propose that each of our pivotal Phase 3 clinical trials will be a double-blinded, randomized placebo-controlled trial. We plan to identify patients through interactions with physicians specializing in the medical management of PWS and to screen all patients for eligibility at their first visit. We expect that patients who qualify for enrollment and who agree to participate in the trial will receive subcutaneous injections of beloranib or placebo twice weekly. We refer to the time at which patients are enrolled and initiate trial drug treatment as baseline.

We propose that the eligibility criteria for inclusion of patients in our planned pivotal Phase 3 clinical trials will include the following:

- Genetically confirmed diagnosis of PWS.
- Age of at least 12 years but not older than 65 years.
- BMI greater than 30 kg/m<sup>2</sup> but less than 60 kg/m<sup>2</sup>, except that for patients between 12 and 18 years of age, we will require a BMI Z-score  $\geq 2$ , which means the juveniles' BMI will be in the 95<sup>th</sup> percentile or higher for children of their age. These BMI criteria define obesity in adult and adolescent individuals, respectively, and we believe that they encompass most PWS patients to allow for a clear assessment of beloranib's impact on body fat content.
- Baseline PWS-HQ score of 13 or greater. A PWS-HQ score of 13 corresponds to moderate behavioral derangement associated with hunger-related behavior typical of PWS. The possible range of scores in the PWS-HQ, as it is anticipated to be employed in our Phase 3 clinical trials, is 0-36. During our Phase 2a clinical trial of beloranib in PWS patients, we observed a floor effect of the PWS-HQ in the clinical response in patients who had PWS-HQ scores lower than 13, which indicates that the instrument may lose sensitivity to drug responses in patients with nominally expressed hyperphagia-related behaviors. As a result, we expect to only include patients with baseline scores of 13 or above. We believe this criterion will reduce variability in clinical response and further improve our ability to detect differences between the beloranib treatment groups and the placebo group for this co-primary endpoint.

We plan to include in our pivotal Phase 3 clinical trials those patients with Type 2 diabetes, a common co-morbid condition in PWS, particularly in older patients, and those patients being treated with growth hormone, a common treatment for patients with PWS to assist in their growth and management of body composition, particularly lean body mass.

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### *Timing of the Planned Pivotal Phase 3 Clinical Program*

Subject to our discussions with the regulatory authorities, we anticipate initiating our planned pivotal Phase 3 clinical trial in the United States in the second half of 2014. After initiation, it will likely take at least six months to fully enroll up to 90 PWS patients in this trial. We anticipate initiating our Phase 3 clinical trial in the European Union in the first half of 2015. After initiation, it will likely take at least six months to fully enroll up to 150 PWS patients in this trial. We have made preliminary arrangements with a number of clinical sites associated with key opinion leaders in the PWS field to aid the recruitment of an adequate number of patients for our planned pivotal Phase 3 clinical trial in the United States. We anticipate using ten or more trial sites in the United States and a similar number of sites in the European Union. We are currently in the process of identifying CROs to support our planned Phase 3 clinical trials and identifying key opinion leaders in the PWS field to aid in the recruitment of an adequate number of patients for our planned pivotal Phase 3 clinical trial in the European Union.

Before we initiate our planned pivotal Phase 3 clinical program, we must also manufacture our clinical trial materials, including drug product, placebo and other aspects of the dosing kit. We anticipate these will be available during the third quarter of 2014. We have selected a vendor we intend to use for quality assurance/control, consolidation and centralized analysis of data obtained from DEXA scans across different trial sites for the purpose of assessing total body fat content and other body composition endpoints. In addition, the FDA may suggest toxicology studies in species other than the rat and dog, which we recently completed. Any such additional toxicology studies must be completed prior to the initiation of our planned pivotal Phase 3 clinical trials.

### *Other Clinical Trials*

We also plan to assess the utility of beloranib in the treatment of patients with craniopharyngioma-associated obesity through a Phase 2a clinical trial, beginning in the first half of 2014. This clinical trial, a four-week, multicenter, clinical trial to be conducted in Australia and the United States, is planned to assess the impact of 1.8 mg beloranib or placebo on body weight, body composition and hunger. We intend to initiate a Phase 2b clinical trial of beloranib as a treatment for severe obesity in the general population. Through these efforts, combined with advances in non-clinical development of beloranib, we aspire to establish a regulatory strategy that will allow commercialization of beloranib.

### **Pre-clinical**

We conducted toxicology studies of beloranib in support of clinical development. Dose selection and precautions for ongoing clinical trials have been informed by toxicology studies in beagle dogs, rats and rabbits. In our dog studies we observed hypospermatogenesis, or low sperm counts, lowering of platelets, decreased white blood cell counts, gastrointestinal bleeding and seizures, all of which were reversible and occurred at doses and exposures above the human dose. The most sensitive changes were mild and reversible effects on spermatogenesis occurring at systemic drug exposures two-to-three fold above the human male exposure in the ZAF-201 trial. In our rat studies, we observed a sporadic, minimal and reversible reduction of sperm counts and cellular changes in the testes at exposure levels ten- to 15-fold above the male human exposure in the ZAF-201 trial. During these studies, the margins to the no adverse effect levels in females were 50- to 100-fold for rats and 40- to 60-fold for dogs. In addition, embryofetal studies have been conducted in rats that show a one- to two-fold exposure margins to female doses in the ZAF-201 trial. However, no safety margin in our rabbit studies were demonstrated due to minor and variant head and eye malformations.

Given the safety findings in animals, clinical trials of beloranib have included monitoring for blood cell changes, sperm counts, sperm morphology and hormones in men, as well as frequent pregnancy testing and requirement for redundant, implanted or surgical methods of birth control in women. To date, the clinical findings have shown no evidence of the hematological or male reproductive findings in humans, thus verifying the margins indicated in the animal species and no pregnancies have occurred. We believe that, as with other anti-obesity drugs, if approved, beloranib will carry a Category X label and be contraindicated in pregnant women or women looking to become pregnant.



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We recently completed long-term toxicology studies of six-month duration in the rat and nine-month duration in the dog that we will submit to the FDA to support clinical trial durations of one year or more. The FDA will determine whether it will suggest additional toxicology studies in another species after it has reviewed these studies. We will also be testing beloranib for potential immunotoxicology and phototoxicity. We plan to initiate such additional toxicology studies prior to the initiation of our planned Phase 3 clinical program in PWS patients. We have initiated dose-ranging studies in preparation for two-year carcinogenicity studies in the mouse and rat, which will begin in 2014. Given that PWS manifests during childhood, we plan to conduct juvenile safety studies starting in 2014 that will allow for testing and eventual marketing in the juvenile population.

### **Future Product Candidates**

We have been working since our inception in 2005 to explore and pursue new molecules leveraging the therapeutic effects of MetAP2 inhibitors in metabolic diseases including severe obesity, type 2 diabetes and NASH. As a direct result of medicinal chemistry efforts oriented to the identification of best in class MetAP2 inhibitors, we have identified compounds of use as potential back-up or follow-on compounds supporting beloranib, as well as novel inhibitors with improved pharmacological and physicochemical features. We continue to explore the utility of these molecules as a component of our program, and have identified a range of candidate molecules being prepared for advancement into early development.

As a part of this effort, we conducted a medicinal chemistry discovery program to find reversible inhibitors of MetAP2 that could be delivered orally and applied broadly across multiple areas of unmet medical need. The program delivered over 250 molecules in seven molecular families, and ZGN-839 was selected from this collection as a potent inhibitor with drug-like properties. In pre-clinical studies, ZGN-839 lowered body weight by approximately 9% after 16 days of treatment versus control animals and reduced plasma cholesterol and glucose, along with improvements in liver fat and the weight of abdominal adipose tissue in mice that were otherwise obese and insulin resistant due to long-term exposure to a high fat, obesogenic, diet. Further, in a mouse model of diabetes and NASH, ZGN-839 treatment for four weeks reduced the severity of NASH and reduced plasma glucose. We believe that compounds like ZGN-839 will have utility in the treatment of type 2 diabetes in humans, and will further cause improvements in cardiovascular risk factors including low density lipoprotein cholesterol.

A synthetic process to produce ZGN-839 for safety testing and clinical trials is currently under development. We currently plan to conduct IND-enabling studies of ZGN-839 in 2014 and to file an IND in the United States to begin clinical development of ZGN-839 beginning in the first half of 2015.

### **Manufacturing and Supply**

Beloranib is a small molecule drug that is synthesized with readily available raw materials using conventional chemical processes. The current process to produce beloranib for clinical trials involves (i) synthesis of crystalline drug substance, (ii) production of sterile crystalline drug substance, (iii) particle size control, formulation and vialing of active drug product, (iv) production and vialing of a sterile diluent and (v) production and vialing of a sterile placebo. We are currently in the process of manufacturing finished drug product for use in our upcoming clinical trials. Sterile drug substance is currently in hand. Finished drug product, diluent and placebo are expected to be available in the third quarter of 2014. Aside from our planned Phase 2a clinical trial in patients with obesity caused by craniopharyngioma, we will not be able to commence any additional clinical trials without the production of additional finished drug product. The manufacturing process is under active development and these projections could change based on delays encountered with manufacturing activities, equipment scheduling and material lead times. Additionally, we will work to establish a convenient dosing form of beloranib to improve the utility, look, convenience and feel of beloranib for patients—for example a pen injector system with single-use disposable cartridges.

We currently have no manufacturing facilities and limited personnel with manufacturing experience. We rely on contract manufacturers to produce both drug substance and drug product required for our clinical trials. No long-term supply agreements are in place with our contractors, and each batch is individually contracted



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under a quality and supply agreement. If we engage new contractors, such contractors must be approved by the FDA and other comparable foreign regulatory agencies. We plan to continue to rely upon contract manufacturers and, potentially, collaboration partners to manufacture commercial quantities of beloranib, if approved. Our current scale of manufacturing is adequate to support all of our needs for clinical trial supplies and launch for orphan markets. For peak usage in orphan markets and for indications with larger populations, we will need to identify contract manufacturers or partners to produce beloranib on a larger scale.

### **Sales and Marketing**

We recently hired a Chief Commercial Officer, however, given our stage of development, we have not yet established a commercial organization or distribution capabilities, nor have we entered into any partnership or co-promotion arrangements with an established pharmaceutical company. To develop the appropriate commercial infrastructure to launch beloranib, we may either do so on our own or by establishing alliances with one or more pharmaceutical company collaborators, depending on, among other things, the applicable indications, the related development costs and our available resources.

### **Licenses**

#### ***CKD License***

In July 2009, we entered into an Exclusive License Agreement with Chong Kun Dang Pharmaceutical Corp. of South Korea, or CKD, pursuant to which we exclusively licensed beloranib from CKD on a worldwide basis, with the exception of South Korea. In consideration of such exclusive license, we paid an initial license fee to CKD, paid a one-time fee following initiation of a proof of concept trial, agreed to make milestone payments of up to \$30.0 million (of which \$1.0 million has been paid) to CKD upon the achievement of certain specified events, and agreed to pay a portion of sublicensing income to CKD. Furthermore, if we receive marketing approval for beloranib, we will pay single-digit royalties to CKD based on annual net sales of beloranib on a country-by-country and product-by-product basis until the later to occur of (i) the expiration of the last to expire patent in such country within the CKD patent rights containing a valid claim covering beloranib or its use for which regulatory approval has been obtained in such country, or (ii) ten years from the first commercial sale of beloranib in such country. Pursuant to this agreement, we committed to using commercially reasonable efforts to develop and commercialize beloranib. This agreement will remain in effect on a country-by-country and product-by-product basis until royalties are no longer due in such country, subject to earlier termination by either party upon mutual consent, or in the event of uncured breach or insolvency on the part of the other party, or by us for any reason up to 60 days' prior notice.

#### ***Children's License***

In January 2007, we entered into an Exclusive License Agreement with Children's Medical Center Corporation, or Children's, pursuant to which we exclusively licensed certain patent rights from Children's on a worldwide basis. The licensed patent rights relate to decreasing the growth of fat tissue, and thereby cover the use of beloranib and related molecules as anti-obesity agents. In consideration of such exclusive license, we paid an initial license fee upon execution of the license to Children's and annual maintenance fees through the fifth anniversary of the date of the license. We also agreed to make milestone payments to Children's of up to \$2.7 million (of which \$0.2 million has been paid) with respect to the first licensed product and up to \$1.3 million with respect to each subsequent licensed product, if any, that is a new chemical entity upon the achievement of certain specified events and to pay a portion of sublicensing income to Children's. If we receive marketing approval for beloranib, we will pay single-digit royalties to Children's based on net sales of beloranib until the later to occur of (i) the expiration of the last to expire patent in such country within the licensed patents containing a valid claim covering beloranib or (ii) 15 years from the date of the agreement. This agreement will remain in effect for the longer of (i) 15 years and (ii) the life of the last expiring licensed patent, subject to earlier termination (x) by Children's in the event of our insolvency or our failure to cure a breach within 60 days (30 days in the case of non-payment) of receiving written notice thereof, or (y) by us for any reason upon 120 days' prior written notice.

## **Intellectual Property**

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking and maintaining patents intended to cover our products and compositions, their methods of use and any other inventions that are important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain the proprietary position of beloranib and our other development programs.

Our owned and licensed patents and patent applications relate to beloranib compositions of matter, formulations, polymorphs, methods of treating obesity using dosing regimens of beloranib and methods of treating hypothalamic obesity. The issued U.S. and European patents generally directed to beloranib compositions of matter are exclusively licensed and will each expire in 2019. We own an issued U.S. patent relating to beloranib polymorph compositions of matter that will expire in 2031 and an issued U.S. patent to methods of treating obesity that will expire in 2029. We own pending patent applications in Europe to beloranib polymorph composition of matter and methods of treating obesity that we expect to expire, once issued, in 2031.

As of February 28, 2014, we own two issued U.S. patents, eight pending U.S. patent applications and foreign counterpart applications, and one Patent Cooperation Treaty, or PCT, application that will allow us to seek corresponding protection worldwide, all of which relate to beloranib. We have a license to two U.S. issued patents, one with corresponding issued foreign counterpart patents, that also relate to beloranib. We also co-own one patent application relating to methods of using beloranib with an option to exclusively license the co-owner rights.

As of February 28, 2014, we own seven pending U.S. patent applications with pending foreign counterpart applications and five PCT patent applications, all of which relate to our MetAP2 inhibitor program. Of these, one pending U.S. patent application with pending foreign counterpart patent applications and one PCT patent application relate to our early-stage product candidate ZGN-839.

As of February 28, 2014, we own two pending U.S. patent applications with pending foreign counterpart patent applications, one pending PCT patent application and two U.S. provisional patent applications that relate to our second-generation MetAP2 inhibitor program.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the non-provisional application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or U.S. PTO, in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period. However, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also twenty years from the earliest effective filing date. Our issued patents will expire on dates ranging from 2019 to 2031. However, the actual protection afforded by a patent varies on a claim by claim and country to country basis for each applicable product and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

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Furthermore, the patent positions of biotechnology and pharmaceutical products and processes like those we intend to develop and commercialize are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in such patents has emerged to date in the United States. The patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries can diminish our ability to protect our inventions, and enforce our intellectual property rights and more generally, could affect the value of intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to maintain and solidify our proprietary position for our drugs and technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of the patent applications that we may file or license from third parties will result in the issuance of any patents. The issued patents that we own or may receive in the future, may be challenged, invalidated or circumvented, and the rights granted under any issued patents may not provide us with proprietary protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may be able to independently develop and commercialize similar drugs or duplicate our technology, business model or strategy without infringing our patents. Because of the extensive time required for clinical development and regulatory review of a drug we may develop, it is possible that, before any of our drugs can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent.

As a result of the America Invents Act of 2011, the United States transitioned to a first-inventor-to-file system in March 2013, under which, assuming the other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent. This will require us to minimize the time from invention to the filing of a patent application.

We may rely, in some circumstances, on trade secrets and unpatented know-how to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our consultants, scientific advisors and contractors and invention assignment agreements with our employees. 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 known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use 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. For more information, See “Risk Factors—Risks Related to our Intellectual Property.”

Our commercial success will also depend in part on not infringing the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our drugs or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future drugs may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the U.S. PTO, to determine priority of invention.

In addition, substantial scientific and commercial research has been conducted for many years in the areas in which we have focused our development efforts, which has resulted in third parties having a number of issued patents and pending patent applications. Patent applications in the United States and elsewhere are published only after 18 months from the priority date. The publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made. Therefore, patent applications relating to drugs similar to beloranib and any future drugs, discoveries or technologies we might develop may have already been filed by others without our knowledge.

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### **Competition**

The biopharmaceuticals industry is highly competitive. There are many public and private biopharmaceutical companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our product candidates or address similar markets. It is probable that the number of companies seeking to develop products and therapies similar to our products will increase. Many of these and other existing or potential competitors have substantially greater financial, technical and human resources than we do and may be better equipped to develop, manufacture and market products. These competitors may develop and introduce products and processes comparable or superior to ours.

#### ***Obesity Caused by Rare Conditions***

There are no current pharmacological treatments for regulating hunger and hyperphagia-related behaviors of PWS patients and patients with craniopharyngioma-associated obesity, and bariatric surgery is contraindicated in PWS patients and not frequently employed in patients with craniopharyngioma-associated obesity. We are aware of a clinical trial planned by Ferring Pharmaceuticals, Inc. to evaluate the use of oxytocin, a brain peptide hormone hypothesized to increase trust, reduce anxiety and improve behavior in patients with PWS. We also are aware of a clinical trial being planned by Essentialis, Inc. to evaluate the safety and tolerability of controlled-release diazoxide in PWS patients and to explore the effects of diazoxide on hyperphagia-related behaviors and energy expenditure. We are not aware of any clinical trials of drugs specifically targeting patients with craniopharyngioma-associated obesity.

#### ***Severe Obesity in the General Population***

##### *Surgical Approaches*

Surgical approaches to treat severe obesity are becoming increasingly accepted and are believed to be the main form of competition to beloranib in this indication. Bariatric surgery, including gastric bypass and gastric banding procedures, is typically employed for obese patients with a BMI exceeding 40 kg/m<sup>2</sup> or those with a BMI greater than 30 kg/m<sup>2</sup> who are experiencing obesity-related complications such as diabetes. However, in December 2010, the FDA's Advisory Committee for Gastroenterology and Urology Devices convened and voted in favor of recommending to the FDA that gastric banding procedures be approved for obese patients with a BMI greater than 30 kg/m<sup>2</sup> who are experiencing obesity related co-morbidities or patients with a BMI greater than 35 kg/m<sup>2</sup> with or without obesity related co-morbidities. In addition, other potential approaches which utilize various implantable devices or surgical tools are in development, by companies such as Allergan, Inc., Boston Scientific Corporation, Covidien Ltd., EnteroMedics, Inc., GI Dynamics, Inc., Johnson & Johnson and Medtronic, Inc.

##### *Existing Obesity Drugs*

In addition, beloranib will compete with orlistat, phentermine/topiramate and lorcaserin, three recently approved and currently marketed pharmaceutical products in the United States for the treatment of obesity, and several older agents, indicated for short-term administration, phentermine, phendimetrazine, benzphetamine and diethylpropion. Orlistat is marketed in the United States by Roche Group under the brand name Xenical and over-the-counter in the United States at half the prescribed dose by GlaxoSmithKline under the brand name alli. In June 2013, Arena Pharmaceuticals, Inc. launched its lorcaserin product, which is marketed in the United States under the name Belviiq and in September 2012, Vivus, Inc. commercially launched its combination product, phentermine/topiramate, under the trade name Qsymia.

Despite the large market opportunity for anti-obesity agents, there are relatively few competitive products in late-stage clinical development. Other companies pursuing pharmaceutical treatments for obesity include Neurosearch A/S, Novo Nordisk A/S and Takeda Pharmaceutical Company Limited. In addition, Orexigen Therapeutics, Inc. resubmitted its NDA for Contrave in December 2013.

We are not aware of any clinical trials of drugs specifically targeting patients with severe obesity.

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### **Government Regulation**

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug products such as beloranib. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review and approved by the regulatory authority.

#### ***U.S. Drug Development***

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. 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, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- Completion of extensive nonclinical, sometimes referred to as pre-clinical laboratory tests, pre-clinical animal studies and formulation studies in accordance with applicable regulations, including the FDA's Good Laboratory Practice, or GLP, regulations;
- 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 in accordance with applicable IND and other clinical trial-related regulations, sometimes referred to as current good clinical practices, or cGCPs, to establish the safety and efficacy of the proposed drug for its proposed indication;
- Submission to the FDA of an NDA, for a new drug;
- A determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;
- Satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA's current good manufacturing practice requirements, or cGMP, to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- Potential FDA audit of the pre-clinical and/or clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

The data required to support an NDA is generated in two distinct development stages: pre-clinical and clinical. For new chemical entities, the pre-clinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing. The conduct of the pre-clinical tests must comply with federal regulations, including GLPs. The sponsor must submit the results of the pre-clinical tests, together with manufacturing information, analytical data, any available

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clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on 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. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

The clinical stage of development involves the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed 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. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

Clinical trials are generally conducted in three sequential phases that may overlap, known as Phase 1, Phase 2 and Phase 3 clinical trials. Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug. Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy. Phase 3 clinical trials generally involve large numbers of patients at multiple sites, in multiple countries (from several hundred to several thousand subjects) and are designed to provide the data necessary to demonstrate the efficacy of the product for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of Phase 4 clinical trials.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, 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 if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for

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whether or not a trial may move forward at designated check points based on access to certain data from the trial. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final drug 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.

### *NDA and FDA Review Process*

Following trial completion, trial data is analyzed to assess safety and efficacy. The results of pre-clinical studies and clinical trials are then submitted to the FDA as part of an NDA, along with proposed labeling for the product and information about the manufacturing process and facilities that will be used to ensure product quality, results of analytical testing conducted on the chemistry of the drug, and other relevant information. The NDA is a request for approval to market the drug and must contain proof of safety, purity, potency and efficacy, which is demonstrated by extensive pre-clinical and clinical testing. The application includes both negative or ambiguous results of pre-clinical and clinical trials as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational drug product to the satisfaction of the FDA. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. FDA approval of an NDA must be obtained before a drug may be offered for sale in the United States.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fee schedule, effective through September 30, 2014, the user fee for an application requiring clinical data, such as an NDA, is \$2,169,100. PDUFA also imposes an annual product fee for human drugs (\$104,060) and an annual establishment fee (\$554,600) on facilities used to manufacture prescription drugs. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has 10 months from the filing date in which to complete its initial review of a standard NDA and respond to the applicant, and six months from the filing date for a priority NDA. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and



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under what conditions. In the case of obesity drugs, the FDA normally refers such drugs to the Endocrinologic and Metabolic Drugs Advisory Committee. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and us during the review process. The review and evaluation of an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, pre-clinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information is 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.

There is no assurance that the FDA will ultimately approve a drug product for marketing in the United States and we may encounter significant difficulties or costs during the review process. If a product receives marketing 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 or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 testing which involves clinical trials designed to further assess a drug safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a REMS to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

### ***Orphan Drug Designation***

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means



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that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the European Union has similar, but not identical, benefits.

### *Expedited Development and Review Programs*

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a Fast Track product at any time during the clinical development of the product. Unique to a Fast Track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it will require such post-marketing restrictions as it deems necessary to assure safe use of the drug, such as:

- distribution restricted to certain facilities or physicians with special training or experience; or
- distribution conditioned on the performance of specified medical procedures.

The limitations imposed would be commensurate with the specific safety concerns presented by the drug. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

***Pediatric Trials***

Recently, the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was signed into law on July 9, 2012, amended the FDCA. FDASIA requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs.

***Post-Marketing Requirements***

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the product, providing the regulatory authorities with updated safety and efficacy information, product sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses. Modifications or enhancements to the product or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, which may or may not be received or may result in a lengthy review process.

Prescription drug advertising is subject to federal, state and foreign regulations. In the United States, the FDA regulates prescription drug promotion, including direct-to-consumer advertising. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Any distribution of prescription drug products and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or the PDMA, a part of the FDCA.

In the United States, once a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture 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. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them.

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problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the product from the market.

The FDA also may require post-approval testing, sometimes referred to as Phase 4 testing, risk minimization action plans and post-marketing surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

### ***Other Regulatory Matters***

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments. In the United States, sales, marketing and scientific/educational programs must also comply with state and federal fraud and abuse laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Health Care Reform Law, as amended by the Health Care and Education Affordability Reconciliation Act, or ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or efficacy of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

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### ***U.S. Patent Term Restoration and Marketing Exclusivity***

Depending upon the timing, duration and specifics of the FDA 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 one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the 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. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Marketing exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent 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 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 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an 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, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the pre-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

### ***European Union Drug Development***

In the European Union, our future products may also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of pre-clinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the European Union clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the European Union Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes.

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Under the current regime, before a clinical trial can be initiated it must be approved in each of the European Union countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The European Union clinical trials legislation is currently undergoing a revision process mainly aimed at uniforming and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials, and increasing their transparency.

### ***European Union Drug Review and Approval***

In the European Economic Area, or EEA, (which is comprised of the 27 Member States of the European Union (excluding Croatia) plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

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

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e. in the RMS and the Member States Concerned).

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

### ***European Union New Chemical Entity Exclusivity***

In the European Union, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the

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scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

### ***European Union Orphan Designation and Exclusivity***

In the European Union, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the medicinal product.

In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following medicinal product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

### **Reimbursement**

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidate or a decision by a third-party payor to not cover our product candidate could reduce physician usage of the product candidate and have a material adverse effect on our sales, results of operations and financial condition.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in

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2012 by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our product candidate, if any such product or the condition that it is intended to treat is the subject of a trial. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidate. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Health Care Reform Law, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, or collectively the ACA, enacted in March 2010, is expected to have a significant impact on the health care industry. The ACA is expected to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, the ACA is expected to expand and increase industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare Part D program. We cannot predict the impact of the ACA on pharmaceutical companies as many of the ACA reforms require the promulgation of detailed regulations implementing the statutory provisions which has not yet occurred. For example, pharmaceutical manufacturers are required to track certain financial arrangements with physicians and teaching hospitals, including any "transfer of value" made or distributed to such entities, as well as any investment interests held by physicians and their immediate family members. Manufacturers are required by ACA to begin tracking this information in 2013 and to report this information to CMS beginning in 2014.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA 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. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, started in April 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. The ATRA, among other things, also reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. We expect that additional 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, and in turn could significantly reduce the projected value of certain development projects and reduce our profitability.

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

## **Employees**

As of February 28, 2014, we employed ten full-time employees, including six in research and development and four in general and administrative, and two part-time employees in general and administrative. We have

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never had a work stoppage, and none of our employees is represented by a labor organization or under any collective-bargaining arrangements. We consider our employee relations to be good.

**Facilities**

We lease our office space, which consists of 2,625 square feet located in Cambridge, Massachusetts. Our lease expired on January 31, 2014, under an extended six-month term, but we extended the lease pursuant to the terms of the current lease agreement for an additional six-month period, which commenced on February 1, 2014. We have an opportunity to extend for one more six-month extension under the current lease agreement, which if extended would commence on August 1, 2014. We believe our current office space is sufficient to meet our needs until the expiration of our lease.

**Legal Proceedings**

As of the date of this prospectus, we were not party to any legal matters or claims. In the future, we may become party to legal matters and claims arising in the ordinary course of business, the resolution of which we do not anticipate would have a material adverse impact on our financial position, results of operations or cash flows.



## MANAGEMENT

### Executive Officers, Key Employees and Directors

The following table sets forth certain information about our executive officers, key employees and directors, including their ages as of April 15, 2014.

Name	Age	Position(s)
<b>Executive Officers:</b>		
Thomas E. Hughes, Ph.D.	54	President, Chief Executive Officer and Director
Dennis D. Kim, M.D., M.B.A.	44	Chief Medical Officer
Patricia L. Allen	52	Chief Financial Officer
Alicia Secor	51	Chief Commercial Officer
<b>Key Employees:</b>		
James E. Vath, Ph.D.	53	Head of Research and Development
<b>Directors:</b>		
Peter Barrett, Ph.D.	61	Chairman
Bruce Booth, Ph.D.	40	Director
Avi Goldberg	38	Director
John L. LaMattina, Ph.D.	64	Director
Kevin P. Starr	51	Director
Lou Tartaglia, Ph.D.	50	Director

- (1) Member of the Compensation Committee.
- (2) Member of the Audit Committee.
- (3) Member of the Nominating and Corporate Governance Committee.

The following paragraphs provide information as of the date of this prospectus about our executive officers, key employees and directors. The information presented includes information about each of our directors' specific experience, qualifications, attributes and skills that led our board of directors to the conclusion that he should serve as a director.

*Thomas E. Hughes, Ph.D.* Dr. Hughes has served as our Chief Executive Officer, President and a member of our board of directors since October 2008. From 1987 to 2008, he held several positions at Novartis AG (and formerly Sandoz Pharmaceuticals) including vice president and global head of the cardiovascular and metabolic diseases therapeutic area at the Novartis Institutes for BioMedical Research in Cambridge, MA. In these roles he oversaw many drug discovery and development projects targeting obesity, diabetes and heart disease. Dr. Hughes is the author of over 40 peer-reviewed publications and is an inventor on numerous issued and pending patents related to the treatment of diabetes, cardiovascular disease and obesity. Dr. Hughes also serves as a director on the board of Miragen Therapeutics, Inc., and is a member of several scientific and strategic advisory boards, including Broadview Ventures and Nimbus Discovery, LLC. Dr. Hughes holds a Ph.D. in nutritional biochemistry from Tufts University, an M.S. in Zoology from Virginia Polytechnic Institute & State University and a B.A. in biology from Franklin and Marshall College. Dr. Hughes' qualifications to sit on our board of directors include his extensive knowledge of the obesity industry combined with his leadership, executive, managerial and pharmaceutical company experience, and his more than 25 years of industry experience in the development and commercialization of pharmaceutical products.

*Dennis D. Kim, M.D., M.B.A.* Dr. Kim has served as our Chief Medical Officer since September 2011. From 2001 to 2012, Dr. Kim was an assistant professor of medicine, division of endocrinology/metabolism, at the University of California, San Diego School of Medicine. From September 2008 to February 2011, Dr. Kim held multiple senior-level clinical and corporate affairs positions at Orexigen Therapeutics, a biopharmaceutical company focused on the treatment of obesity, including senior vice president, head of obesity/metabolic diseases; senior vice president, corporate development; and senior vice president, medical affairs and communications. Prior to Orexigen, from September 2007 to September 2008, he was chief medical officer and vice president of

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medical affairs at EnteroMedics, Inc., where he oversaw all aspects of clinical affairs and successfully implemented an initial public offering as part of the executive team in 2007. Previously, from July 2001 to September 2007, he held positions of increasing responsibility at Amylin Pharmaceuticals, Inc., most recently as executive director, corporate strategy, where he managed corporate and business strategic planning spanning all commercial products, developmental drug candidates, corporate alliance partnership and manufacturing support. Dr. Kim holds an M.D. from the University of Health Sciences, The Chicago Medical School, an M.B.A from University of California, San Diego Rady School of Management and a B.S. in biology from the University of California at Los Angeles.

*Patricia L. Allen.* Ms. Allen has served as our Chief Financial Officer since January 2013. Ms. Allen has over 20 years of financial leadership experience in the biotechnology industry at both publicly traded and private companies. From 2011 to 2012, she provided independent consulting services to biotechnology companies in a variety of areas, including interim CFO services, fundraising, deal structures, financial planning, organizational structure, investor relations and business development. Previously, from 2004 to 2011, Ms. Allen served as the Vice President of Finance, Treasurer and Principal Financial Officer of Alnylam Pharmaceuticals, where she had significant interactions with the investment community and was influential in raising over \$900 million via the company's initial public offering, follow-on common stock offerings and multiple business development transactions with top-tier pharmaceutical companies. Prior to Alnylam, Ms. Allen was at Alkermes, Inc., most recently as the Director of Finance. Ms. Allen began her career as an auditor at Deloitte & Touche, LLP. Ms. Allen graduated summa cum laude from Bryant College with a B.S. in business administration.

*Alicia Secor.* Ms. Secor has served as our Chief Commercial Officer since January 2014. She brings over 20 years of pharmaceutical, biotechnology, and medical device experience. Ms. Secor has an established track record in leading the commercial development, and global expansion of products through various stages of life-cycle development, including pre-launch and late-stage commercial phases spanning multiple therapeutic areas including metabolic diseases. From August 2013 to October 2013, she served as Senior Vice President and Chief Operating Officer of Synageva BioPharma Corp. Previously, from November 1998 to July 2013, Ms. Secor spent 15 years at Genzyme Corporation, a Sanofi Company, where she held various leadership positions, most recently as Vice President and General Manager of Metabolic Diseases, a global business consisting of five marketed products, including two products for orphan diseases. Prior to this role, she was Vice President and General Manager of Biosurgical Specialties, a surgical device business focused on adhesion prevention and other novel applications for biomaterials. During her tenure at Genzyme, she was instrumental in advancing products through clinical development and responsible for establishing and executing the commercial development and launch, general management and global expansion. Ms. Secor successfully led multiple strategic business development transactions, held global P&L responsibility, and built high performance teams, resulting in consistent growth and profitability across multiple businesses. Prior to Genzyme, Ms. Secor held positions at Alkermes plc in business development, at Centocor, Inc. (a Johnson & Johnson Company) in clinical and commercial operations, and began her career at Pfizer Inc. as a hospital-based sales representative. She received her M.B.A. from Northeastern University, and her B.S. in Healthcare Administration from the University of New Hampshire.

*James E. Vath, Ph.D.* Dr. Vath has served as our Head of Research and Development since 2006. From July 2006 to 2008, Dr. Vath served as our Chief Scientific Officer. Dr. Vath has over 20 years of experience in the biotechnology and pharmaceutical industries. Prior to joining the company, from 2004 to 2005, Dr. Vath served as senior vice president of product development at Phylogix Inc. where he created and implemented the corporate operational and R&D plan for the lead product in oncology-supportive care. Prior to Phylogix, from 1999 to 2004, he served in multiple roles, most recently as senior vice president of research at Praecis Pharmaceuticals where he led the R&D organization through multiple IND filings and a product approval. From 1996 to 1999 Dr. Vath was at Millennium Pharmaceuticals where he was most recently Director of Protein Technologies and from 1989 to 1996 he was a laboratory head in the development organization at Genetics Institute. Dr. Vath is a contributing author on numerous peer-reviewed journal publications and book chapters. Dr. Vath holds a Ph.D. in chemistry from the Massachusetts Institute of Technology and a B.S. in chemistry from Northeastern University.

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*Peter Barrett, Ph.D.* Dr. Barrett has served as the chairman of our board of directors since August 2006. Dr. Barrett joined Atlas Venture, an early-stage venture capital fund, in 2002, and currently serves as a partner in the life sciences group. Previously, from 1998 to 2002, he was a co-founder, executive vice president and chief business officer of Celera Genomics. Prior to Celera, from 1979 to 1998, Dr. Barrett held senior management positions at the Perkin-Elmer Corporation, most recently serving as vice president, corporate planning and business development. Dr. Barrett served on the boards of directors of SciClone Pharmaceuticals, Inc. from 2011 to 2013, and Helios BioSciences Corporation from 2003 to 2012. Dr. Barrett currently serves on the boards of directors of the Perkin-Elmer Corporation and several other privately held companies. Dr. Barrett is currently vice chairman of the advisory council of the Barnett Institute of Chemical and Biological Analysis at Northeastern University, as well as adjunct professor at the Barnett Institute. He also serves as president of the Autism Consortium, a non-profit institution and is a member of the research council at Boston Children's Hospital. Dr. Barrett holds a B.S. in chemistry from Lowell Technological Institute (now known as the University of Massachusetts, Lowell) and a Ph.D. in analytical chemistry from Northeastern University. He also completed Harvard Business School's Management Development Program. Dr. Barrett's qualifications to sit on our board include his extensive leadership, executive, managerial and business experience with life sciences companies, including experience in the formation, development and business strategy of multiple start-up companies in the life sciences sector.

*Bruce Booth, Ph.D.* Dr. Booth has served as a member of our board of directors since August 2006. Dr. Booth joined Atlas Venture in 2005, and currently serves as partner in the life sciences group. Previously, from 2004 to 2005, Dr. Booth was a principal at Caxton Health Holdings L.L.C., a healthcare-focused investment firm, where he focused on the firm's venture capital activities. Prior to Caxton, from 1999 to 2004, he was an associate principal at McKinsey & Company, a global strategic management consulting firm, where he advised clients on R&D productivity, corporate strategy and business development issues across the biopharmaceutical sector. Dr. Booth currently serves on the board of directors of Miragen Therapeutics, Bicycle Therapeutics, Nimbus Discovery, Rodin Therapeutics and several other seed-stage biotechnology companies. In addition, Dr. Booth serves on UCB Pharma's New Medicines Scientific Advisory Board, and participates on several other advisory boards for pharmaceutical companies and academic medical centers. Dr. Booth is also a trustee of the New York Academy of Medicine. As a British Marshall Scholar, Dr. Booth holds a Ph.D. in molecular immunology from the Oxford University's Nuffield Department of Medicine and a B.S. in biochemistry, summa cum laude, from the Pennsylvania State University. Dr. Booth's qualifications to sit on our board include his extensive leadership, executive, managerial and business experience with life sciences companies, including experience in the formation, development and business strategy of multiple start-up companies in the life sciences sector.

*Avi Goldberg.* Mr. Goldberg has served as a member of our board of directors since November 2005. Since 2005, Mr. Goldberg has served as partner at Greatpoint Ventures. Mr. Goldberg served as the chief operating officer at GreatPoint Energy from 2004 to 2013, where he was responsible for managing all business development, legal, financial and operational planning functions for the company. Previously, from 2000 to 2004, Mr. Goldberg co-founded Coatue Corporation, a microelectronics company developing novel polymer materials for use in the semiconductor industry. As the chief operating officer and member of the board of directors, he was instrumental in assembling the executive team, securing venture and debt financing, and negotiating the purchase of the company in June 2003 by Advanced Micro Devices. From 1998 to 2000, Mr. Goldberg served as director of worldwide sales and network optimization for Cignal Global Communications, a pioneer in voice over data network communications, where he managed global sales and cost containment for Cignal's core business units, generating over \$50 million a year in revenue. Mr. Goldberg graduated magna cum laude from Boston University with a B.A. in political science and strategic intelligence. Mr. Goldberg's qualifications to sit on our board include his extensive operating and managerial experiences.

*John L. LaMattina, Ph.D.* Dr. LaMattina has served as a member of our board of directors since December 2013. Since 2009, Dr. LaMattina has been a senior partner at PureTech Health, a technology development company focusing on biotech investments. Prior to that, Dr. LaMattina spent 30 years at Pfizer Inc. beginning as a medicinal chemist in 1977. During his career, he was appointed to various positions of increasing responsibility for Pfizer

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Central Research, including Vice President of U.S. Discovery Operations in 1993, Senior Vice President of Worldwide Discovery Operations in 1998, Senior Vice President of Worldwide Development in 1999 and President of Pfizer Global R&D in 2003. Dr. LaMattina graduated with cum laude honors from Boston College with a B.S. in Chemistry. He received a Ph.D. from the University of New Hampshire in Organic Chemistry and subsequently was at Princeton University in the National Institutes of Health Postdoctoral Fellowship program. From 2008 to 2012, Dr. LaMattina served on the board of directors of Human Genome Sciences. From 2008 to 2010, Dr. LaMattina served on the board of directors of Neurogen Corp. Dr. LaMattina currently serves on several boards, including the board of directors of Ligand Pharmaceuticals, the Board of Trustees of Boston College, the Scientific Advisory Board for Trevena Pharmaceuticals and the Scientific Advisory Board of Ziarco Pharmaceuticals. Dr. LaMattina's qualifications to sit on our board include his valuable pharmaceutical experience, including his service at Pfizer Inc., one of the world's largest pharmaceutical companies, in addition to his experience on several boards and involvement in the biotechnology industry through his position as a senior partner at PureTech.

*Kevin P. Starr.* Mr. Starr has served as a member of our board of directors since December 2006. In April 2007, Mr. Starr co-founded Third Rock Ventures, a venture capital firm where he remains a partner. From January 2003 to March 2007, Mr. Starr undertook a number of entrepreneurial endeavors in the life science and entertainment industries. From December 2001 to December 2002, Mr. Starr served as chief operating officer of Millennium. He also served as Millennium's chief financial officer from December 1998 to December 2002. Mr. Starr currently serves on the board of directors of Agios Pharmaceuticals, Inc., Alnylam Pharmaceuticals, Inc., PanOptica, Inc., MyoKardia, Inc., Global Blood Therapeutics, Inc., Afferent Pharmaceutical, Ember Therapeutics and SAGE Therapeutics. Mr. Starr received an M.S. in corporate finance from Boston College and a B.S./B.A. in mathematics and business from Colby College. Mr. Starr's qualifications to serve on our board of directors include his executive management roles with responsibility over key financial and business planning functions and experience in the formation, development and business strategy of multiple start-up companies in the life sciences sector.

*Lou Tartaglia, Ph.D.* Dr. Tartaglia has served as a member of our board of directors since October 2007. He joined Third Rock Ventures, a venture capital firm dedicated to building transformational life science companies, in 2007, and currently serves as a partner. Prior to joining Third Rock Ventures, from July 2004 to June 2007, Dr. Tartaglia was senior vice president and general manager at Gene Logic, and from April 1993 to June 2004, he served as vice president of new ventures and vice president of metabolic diseases at Millennium Pharmaceuticals. Dr. Tartaglia holds a Ph.D. in Biochemistry from the University of California, Berkeley and a B.S. in Chemistry from University at Albany, The State University of New York. Dr. Tartaglia's qualifications to sit on our board include his extensive leadership, executive, managerial and business experience with life sciences companies, including experience in the formation, development and business strategy of multiple start-up companies in the life sciences sector.

### **Composition of our Board of Directors**

As of February 28, 2014, our board of directors consisted of seven members, each of whom are members pursuant to the board composition provisions of our certificate of incorporation and our voting agreement, which agreement is described under "Certain Relationships and Related Party Transactions" in this prospectus. These board composition provisions will terminate upon the completion of this offering. Upon the termination of these provisions, there will be no further contractual obligations regarding the election of our directors. Our nominating and corporate governance committee and our board of directors may therefore consider a broad range of factors relating to the qualifications and background of nominees, which may include diversity, which is not only limited to race, gender or national origin. We have no formal policy regarding board diversity. Our nominating and corporate governance committee's and our board of directors' priority in selecting board members is identification of persons who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape and professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal. Our amended and

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restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Notwithstanding the foregoing, Dr. Hughes will serve without further compensation as a member of the board of directors for as long as he serves as our chief executive officer.

*Director Independence.* Our board of directors has determined that all members of the board of directors, except Dr. Hughes, are independent directors, including for purposes of the rules of NASDAQ Stock Market and relevant federal securities laws and regulations. There are no family relationships among any of our directors or executive officers.

*Staggered Board.* In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering, our board of directors will be divided into three staggered classes of directors of the same or nearly the same number and each will be assigned to one of the three classes. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. The terms of the directors will expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2015 for Class I directors, 2016 for Class II directors and 2017 for Class III directors.

- Our Class I directors will be \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_ ;
- Our Class II directors will be \_\_\_\_\_ and \_\_\_\_\_ ; and
- Our Class III directors will be \_\_\_\_\_ and \_\_\_\_\_ .

Our amended and restated certificate of incorporation and amended and restated by-laws provide that the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

### **Committees of our Board of Directors**

Our board of directors plans on establishing an audit committee, a compensation committee and a nominating and corporate governance committee, each of which will operate pursuant to a charter to be adopted by our board of directors and will be effective upon completion of the offering. Upon the completion of this offering, the composition and functioning of all of our committees will comply with all applicable requirements of the Sarbanes-Oxley Act of 2002, the NASDAQ Stock Market and the SEC rules and regulations.

*Audit committee.* Effective upon completion of this offering, \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_ will serve on the audit committee, which will be chaired by \_\_\_\_\_. Our board of directors has determined that \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_ are “independent” for audit committee purposes as that term is defined in the rules of the SEC and the applicable NASDAQ Stock Market rules, and has sufficient knowledge in financial and auditing matters to serve on the audit committee. Our board of directors has designated \_\_\_\_\_ as an “audit committee financial expert,” as defined under the applicable rules of the SEC. Our board has determined that while \_\_\_\_\_ satisfy the independence requirements under applicable NASDAQ Stock Market rules, they do not satisfy the independence requirements of the SEC applicable to members of audit committees. The transition rules of the SEC provide that two members of the audit committee may be exempt from these more stringent independence requirements for 90 days after the effectiveness of this registration statement, and one member may be exempt for \_\_\_\_\_.

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one year after the effectiveness of this registration statement. Our board of directors intends to cause our audit committee to comply with the transition rules within the applicable time periods. The audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our consolidated financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly consolidated financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee's review and discussions with management and our independent registered public accounting firm whether our audited consolidated financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our consolidated financial statements and our compliance with legal and regulatory requirements as they relate to our consolidated financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related person transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases and scripts.

*Compensation committee.* Effective upon completion of this offering, \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_ will serve on the compensation committee, which will be chaired by \_\_\_\_\_. Our board of directors has determined that each member of the compensation committee is "independent" as defined in the applicable NASDAQ Stock Market rules. The compensation committee's responsibilities include:

- annually reviewing and approving corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and determining the compensation of our Chief Executive Officer;
- reviewing and approving the compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and making recommendations to the board of directors with respect to director compensation;
- reviewing and discussing with management the compensation discussion and analysis to be included in our annual proxy statement or Annual Report on Form 10-K; and
- reviewing and discussing with the board of directors the corporate succession plans for the Chief Executive Officer and other key officers.

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*Nominating and corporate governance committee.* Effective upon completion of this offering, \_\_\_\_\_, \_\_\_\_\_ and \_\_\_\_\_ will serve on the nominating and corporate governance committee, which will be chaired by \_\_\_\_\_. Our board of directors has determined that each member of the nominating and corporate governance committee is “independent” as defined in the applicable NASDAQ Stock Market rules. The nominating and corporate governance committee’s responsibilities include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- reviewing the size and composition of the board of directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board’s committees;
- developing and recommending to the board of directors a code of business conduct and ethics and a set of corporate governance guidelines;
- developing a mechanism by which violations of the code of business conduct and ethics can be reported in a confidential manner; and
- overseeing the evaluation of the board of directors and management.

Our board of directors may from time to time establish other committees.

### **Compensation Committee Interlocks and Insider Participation**

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

### **Corporate Governance**

We plan to adopt a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting, which will be effective upon completion of this offering. Upon the completion of this offering, our code of business conduct and ethics will be available on our website at [www.zafgen.com](http://www.zafgen.com). We intend to disclose any amendments to the code, or any waivers of its requirements, on our website or in a Current Report on Form 8-K.

### **Board Leadership Structure and Board’s Role in Risk Oversight**

The positions of chairman of the board and Chief Executive Officer are presently separated and have historically been separated at our company. We believe that separating these positions allows our Chief Executive Officer to focus on our day-to-day business, while allowing the chairman of the board to lead the board of directors in its fundamental role of providing advice to and independent oversight of management. Our board of directors recognizes the time, effort and energy that the Chief Executive Officer is required to devote to his position in the current business environment, as well as the commitment required to serve as our chairman, particularly as the board of directors’ oversight responsibilities continue to grow. While our amended and restated by-laws and corporate governance guidelines do not require that our chairman and Chief Executive Officer positions be separate, our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

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Risk is inherent with every business, and how well a business manages risk can ultimately determine its success. We face a number of risks, including risks relating to our operations, strategic direction and intellectual property as more fully discussed under “Risk Factors” in this prospectus. Management is responsible for the day-to-day management of risks we face, while our board of directors, as a whole and through its committees, has responsibility for the oversight of risk management. In its risk oversight role, our board of directors has the responsibility to satisfy itself that the risk management processes designed and implemented by management are adequate and functioning as designed.

The role of the board of directors in overseeing the management of our risks is conducted primarily through committees of the board of directors, as disclosed in the descriptions of each of the committees above and in the charters of each of the committees. The full board of directors (or the appropriate board committee in the case of risks that are under the purview of a particular committee) discusses with management our major risk exposures, their potential impact on us, and the steps we take to manage them. When a board committee is responsible for evaluating and overseeing the management of a particular risk or risks, the chairman of the relevant committee reports on the discussion to the full board of directors during the committee reports portion of the next board meeting. This enables the board of directors and its committees to coordinate the risk oversight role, particularly with respect to risk interrelationships.



**EXECUTIVE AND DIRECTOR COMPENSATION****Summary Compensation Table**

The following table sets forth the compensation paid or accrued during the fiscal year ended December 31, 2013 to our chief executive officer and our next highest-paid executive officers as of December 31, 2013. We refer to these officers as our named executive officers.

<b>Name and Principal Position</b>	<b>Year</b>	<b>Salary (\$)</b>	<b>Bonus (\$)</b>	<b>Option Awards<sup>(1)</sup> (\$)</b>	<b>Non-Equity Incentive Plan Compensation (\$)</b>	<b>All Other Compensation (\$)</b>	<b>Total (\$)</b>
Thomas E. Hughes, Ph.D. <i>Chief Executive Officer</i>	2013	400,000	120,000	591,961	5,100	—	1,117,061
Dennis D. Kim, M.D., M.B.A. <i>Chief Medical Officer</i>	2013	325,000	82,000	85,342	5,100	—	497,442
Patricia L. Allen <i>Chief Financial Officer</i>	2013	237,898 <sup>(2)</sup>	60,000	225,563	4,620	—	528,081

(1) Amounts represent the aggregate grant-date fair value of option awards granted to our named executive officers in 2013 computed in accordance with FASB ASC Topic 718. The assumptions used in the valuation of these awards are consistent with the valuation methodologies specified in the notes to our consolidated financial statements and discussions in “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included elsewhere in this prospectus. The amounts above reflect our aggregate accounting expense for these awards and do not necessarily correspond to the actual value that will be recognized by the named executive officers.

(2) Represents base salary earned by Ms. Allen for services as our Chief Financial Officer during 2013. Ms. Allen’s annual base salary during this period was \$265,000.

**Narrative to Summary Compensation Table***Employment Arrangements with Our Named Executive Officers*

We have entered into an employment agreement or offer letter with each of our named executive officers in connection with their employment with us. These employment agreements and offer letters provide for “at will” employment.

**Thomas E. Hughes, Ph.D.** On July 25, 2008, we entered into an offer letter with Dr. Hughes for the position of President and Chief Executive Officer. Dr. Hughes’ employment has no specified term, but can be terminated at will by either party. Dr. Hughes currently receives a base salary of \$425,000, which is subject to review and adjustment in accordance with company policy. Dr. Hughes is also eligible for an annual merit bonus with a target bonus opportunity of 35% of his base salary, payable at the discretion of the board of directors, based upon performance. Dr. Hughes is eligible to participate in our employee benefit plans generally available to our executive employees, subject to the terms of those plans.

**Dennis D. Kim, M.D., M.B.A.** On August 23, 2011, we entered into an offer letter with Dr. Kim for the position of Chief Medical Officer. Dr. Kim’s employment has no specified term, but can be terminated at will by either party. Dr. Kim currently receives a base salary of \$350,000, which is subject to review and adjustment in accordance with company policy. Dr. Kim is also eligible for an annual merit bonus with a target bonus opportunity of 30% of his base salary, payable at the discretion of the board of directors, based on performance and the business conditions at the company. Dr. Kim is eligible to participate in our employee benefit plans generally available to our executive employees, subject to the terms of those plans.

**Patricia L. Allen.** On December 10, 2012, we entered into an offer letter with Ms. Allen for the position of Chief Financial Officer. Ms. Allen’s employment has no specified term, but can be terminated at will by either party. Ms. Allen currently receives a base salary of \$275,000, which is subject to review and adjustment in

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accordance with company policy. Ms. Allen is also eligible for an annual merit bonus with a target bonus opportunity of 30% of her base salary, payable at the discretion of the board of directors based on performance. Ms. Allen is also eligible to participate in our employee benefit plans generally available to our executive employees, subject to the terms of those plans.

### *Payments Provided Upon Death or Disability*

Under the terms of Dr. Kim's offer letter, if his employment is terminated by reason of his death or disability, he is entitled to base salary and benefits continuation for two months following his death or disability.

### *Payments Provided Upon Termination for Good Reason or Without Cause*

Pursuant to the terms of their offer letters, each of Dr. Kim and Ms. Allen is eligible to receive two months of base salary and benefits continuation in the event his or her employment is terminated by us without Cause, or he or she terminates his or her employment with Good Reason subject to execution and non-revocation of a general release of claims. "Cause" is defined as dishonesty, embezzlement, misappropriation of assets or property of the company, gross negligence, misconduct, neglect of duties, theft, fraud or breach of fiduciary duty to the company, violation of federal or state securities laws, breach of an employment or other agreement with the company, conviction of a felony or any crime involving moral turpitude or material unsatisfactory performance as determined by our board of directors. "Good Reason" is defined as a material diminution in responsibilities, authority and function, a material reduction in base salary, unless such reduction is pursuant to a salary reduction program affecting substantially all of the senior level employees of the company and does not disproportionately adversely affect him, or a material change in the geographic location at which he or she must regularly work.

In addition, under certain option agreements that we have entered into with our named executive officers, we have agreed that if the named executive officer is terminated by us other than for death or disability or cause (as defined in the respective named executive officer's employment agreement), then such executive officer will have a period to exercise his or her vested options as of the date of termination for a period of three months from the date of the termination or the expiration date of the option, whichever is earlier.

### *Payments Provided Upon a Change of Control*

Pursuant to Dr. Hughes' offer letter, we agreed to make certain equity awards to him in the form of options to purchase common stock, and in the event of a change of control of the company, any unvested stock options will be accelerated such that 100% of the shares underlying such options which would otherwise be unvested at the time of the change of control will become vested upon the change of control. Pursuant to Ms. Allen's offer letter, we agreed to make certain equity awards to her in the form of stock options to purchase common stock, and in the event of a consummation of a change of control of the company within the first 12 months of her employment start date, 25% of the unvested stock options at the time of the change of control will become vested upon the change of control. "Change of control" is defined as the acquisition of beneficial ownership (as defined in Rule 13d-3 of the Exchange Act) directly or indirectly by any individual, corporation, partnership or any other entity or organization other than the company or its affiliates of the company's securities representing a majority or more of the voting power of the company's then outstanding securities, a merger or consolidation with any other corporation or the sale by the company of all or substantially all of its assets.

### *Employee Confidentiality, Non-Competition, Non-Solicitation and Assignment Agreements*

Each of our named executive officers has entered into a standard form agreement with respect to confidential information and assignment of inventions. Among other things, this agreement obligates each named executive officer to refrain from disclosing any of our proprietary information received during the course of employment and to assign to us any inventions conceived or developed during the course of employment. Such agreement also provides that during the period of the named executive officer's employment and for 12 months thereafter, the named executive officer will not compete with us and will not solicit our employees, consultants, customers or suppliers.

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**Outstanding Equity Awards at Fiscal Year End**

The following table presents the outstanding equity awards held by each of our named executive officers as of December 31, 2013.

Name	Option Awards		Option Exercise Price (\$)	Option Expiration Date
	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable		
Thomas E. Hughes, Ph.D.	809,227 <sup>(1)</sup>	—	0.12	12/15/2018
Thomas E. Hughes, Ph.D.	78,000 <sup>(2)</sup>	—	0.12	3/18/2019
Thomas E. Hughes, Ph.D.	837,164	17,836 <sup>(3)</sup>	0.13	3/10/2020
Thomas E. Hughes, Ph.D.	524,874	1,574,625 <sup>(4)</sup>	0.39	6/12/2023
Dennis D. Kim, M.D., M.B.A.	506,250	393,750 <sup>(5)</sup>	0.25	10/10/2021
Dennis D. Kim, M.D., M.B.A.	75,670	227,010 <sup>(6)</sup>	0.39	6/12/2023
Patricia L. Allen	—	800,000 <sup>(7)</sup>	0.39	6/12/2023

- (1) Under the terms of Dr. Hughes' option agreement, the shares vested in 36 equal monthly installments beginning on October 2, 2009 and became fully vested on September 2, 2012.
- (2) Under the terms of Dr. Hughes' stock option agreement, all of the shares became fully vested on March 19, 2009.
- (3) Under the terms of Dr. Hughes' stock option agreement, the remaining unvested shares will vest in equal monthly installments through January 1, 2014.
- (4) Under the terms of Dr. Hughes' stock option agreements, 25% of the shares vested on December 19, 2013 and the remaining unvested shares will vest in equal monthly installments through December 19, 2016.
- (5) Under the terms of Dr. Kim's stock option agreement, the remaining unvested shares will vest in equal monthly installments through September 5, 2015.
- (6) Under the terms of Dr. Kim's stock option agreement, 25% of the shares vested on December 19, 2013 and the remaining unvested shares will vest in equal monthly installments through December 19, 2016.
- (7) Under the terms of Ms. Allen's stock option agreements, 25% of the shares vest on January 2, 2014 and the remaining unvested shares will vest in equal monthly installments through January 2, 2017.

**Director Compensation**

The following table sets forth a summary of the compensation we paid to our nonemployee directors during 2013. Other than as set forth in the table and described more fully below, we did not pay any compensation, reimburse any expense of, make any equity awards or non-equity awards to, or pay any other compensation to any of the other nonemployee members of our board of directors in 2013. We reimburse nonemployee directors for reasonable travel expenses. Dr. Hughes, our President and Chief Executive Officer, receives no compensation for his service as a director, and, consequently, is not included in this table. The compensation received by Dr. Hughes as an employee during 2013 is presented in the "Summary Compensation Table" above.

Name	Fees earned or paid in cash(\$)	Option awards(\$) (1)	Total(\$)
Peter Barrett, Ph.D.	—	—	—
Bruce Booth, Ph.D.	—	—	—
Avi Goldberg	—	—	—
Kevin P. Starr	—	—	—
Lou Tartaglia, Ph.D.	—	—	—
John L. LaMattina, Ph.D.	—	57,460	57,460

- (1) Amounts represent the aggregate grant-date fair value of option awards granted to our directors in 2013 computed in accordance with FASB ASC Topic 718. The assumptions used in the valuation of these awards are consistent with the valuation methodologies specified in the notes to our consolidated financial statements and discussions in "Management's Discussion and Analysis of Financial Condition and Result of Operations."

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included elsewhere in this prospectus. The amounts above reflect our aggregate accounting expense for these awards and do not necessarily correspond to the actual value that will be recognized by the directors.

Our board of directors plans on adopting a nonemployee director compensation policy, that will be effective as of the completion of this offering, that is designed to provide a total compensation package that enables us to attract and retain, on a long-term basis, high caliber nonemployee directors. Under the policy, all nonemployee directors will be paid cash compensation from and after the completion of this offering, as set forth below:

	<u>Annual Retainer</u>
<b>Board of Directors:</b>	
All nonemployee members	\$
Additional retainer for Non-Executive Chairman of the Board	\$
<b>Audit Committee:</b>	
Chairman	\$
Non-Chairman members	\$
<b>Compensation Committee:</b>	
Chairman	\$
Non-Chairman members	\$
<b>Nominating and Corporate Governance Committee:</b>	
Chairman	\$
Non-Chairman members	\$

Under the nonemployee director compensation policy, each person who is initially appointed or elected to the board of directors will be eligible for an option grant to purchase up to \_\_\_\_\_ shares of our common stock under our stock option plan on the date he or she first becomes a nonemployee director, which will vest annually over a \_\_\_\_\_ period. In addition, on the date of the annual meeting of stockholders, each continuing non-employee director who has served on the board of directors for a minimum of six months will be eligible to receive an annual option grant to purchase up to \_\_\_\_\_ shares of our common stock, which will vest in full upon the earlier of the first anniversary of the date of grant or the date of the following annual meeting of stockholders. All of the foregoing options will be granted at fair market value on the date of grant.

### **Compensation Risk Assessment**

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

### **Stock Option Plans**

#### *2006 Stock Option Plan*

The Amended and Restated 2006 Stock Option Plan, or 2006 Stock Option Plan, was approved by our board of directors and our stockholders on February 1, 2006 and was most recently amended on April 26, 2013. Under the 2006 Stock Option Plan, 10,863,864 shares of common stock have been reserved for issuance in the form of incentive stock options, non-qualified stock options, restricted stock, unrestricted stock or any combination of the foregoing. The shares issuable pursuant to awards granted under the 2006 Plan are authorized but unissued shares.

The 2006 Stock Option Plan is administered by our board of directors, which has full power to select the employees, directors and service providers to whom awards will be granted and to determine the specific terms and conditions of each award, subject to the provisions of the 2006 Stock Option Plan.

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The option exercise price of each option granted under the 2006 Stock Option Plan is determined by our board of directors and may not be less than the fair market value of a share of common stock on the date of grant. The term of each option is fixed by the board of directors and may not exceed ten years from the date of grant. The board of directors determines at what time or times each option may be exercised when granting the option.

The 2006 Stock Option Plan provides that, upon a sale transaction of the company, unless provision is made in connection with the sale transaction in the sole discretion of the parties thereto for the assumption or continuation of the awards by the successor entity or substitution of the awards with new awards of the successor entity, with appropriate adjustment, all options not exercised will terminate upon the closing of the sale transaction.

Our board of directors may amend the 2006 Stock Option Plan but no such action may adversely affect the rights of an award holder without such holder's consent. Approval by our stockholders of amendments to the 2006 Stock Option Plan must be obtained if required by law.

As of December 31, 2013, options to purchase 8,228,975 shares of common stock were outstanding under the 2006 Stock Option Plan. Our board of directors has determined not to make any further awards under the 2006 Stock Option Plan following the completion of this offering.

### *2014 Stock Option Plan*

On \_\_\_\_\_, 2014, our board of directors adopted and thereafter our stockholders approved our 2014 Stock Option and Incentive Plan, or 2014 Stock Option Plan, which will become effective upon completing of this offering and will replace the 2006 Stock Option Plan. Our 2014 Stock Option Plan provides us flexibility to use various equity-based incentive and other awards as compensation tools to motivate our workforce. These tools include stock options, stock appreciation rights, restricted stock, restricted stock units, unrestricted stock, performance share awards and cash-based awards. The 2014 Stock Option Plan will become effective immediately prior to the completion of this offering.

We have initially reserved \_\_\_\_\_ shares of common stock for the issuance of awards under the 2014 Stock Option Plan (including \_\_\_\_\_ shares of common stock reserved for issuance under our 2006 Stock Option Plan, which will be added to the shares reserved under the 2014 Stock Option Plan), which will be cumulatively increased by \_\_\_\_\_ % of the number of shares of common stock issued and outstanding on the immediately preceding December 31. This number is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares issuable pursuant to awards granted under the 2014 Stock Option Plan will be authorized but unissued shares or shares that we reacquire. The shares of common stock underlying any awards from the 2014 Stock Option Plan and the 2006 Stock Option Plan that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without any issuance of common stock, expire or are otherwise terminated (other than by exercise) under the 2014 Stock Option Plan will be added back to the shares available for issuance under the 2014 Stock Option Plan.

Under the 2014 Stock Option Plan, stock options or stock appreciation rights with respect to no more than \_\_\_\_\_ shares may be granted to any one individual in any one calendar year and the maximum aggregate number of shares that may be issued in the form of incentive stock options shall not exceed the initial number of shares reserved and available for issuance under the 2014 Stock Option Plan.

The 2014 Stock Option Plan will be administered by the compensation committee of the board of directors. The compensation committee has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of the 2014 Stock Option Plan. Employees, nonemployee directors and other key persons (including consultants) are eligible to receive awards under the 2014 Stock Option Plan.

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The 2014 Stock Option Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and options that do not so qualify. The exercise price of each stock option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant or, in the case of an incentive stock option granted to a 10% owner, less than 110% of the fair market value of our common stock on the date of grant. The term of each stock option will be fixed by the compensation committee and may not exceed ten years from the date of grant (or five years in the case of an incentive stock option granted to a 10% owner). The compensation committee will also determine vesting schedule for granted stock options.

The compensation committee may award stock appreciation rights subject to such conditions and restrictions as it may determine. Stock appreciation rights entitle the recipient to shares of common stock, or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right may not be less than 100% of the fair market value of the common stock on the date of grant.

The compensation committee may award restricted stock or restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment or service with us through a specified vesting period. The compensation committee may also grant cash-based awards to participants subject to such conditions and restrictions as it may determine. Our compensation committee may also grant shares of common stock that are free from any restrictions under the 2014 Stock Option Plan. Unrestricted stock may be granted to participants in recognition of past services or for other valid consideration and may be issued in lieu of cash compensation due to such participant.

The compensation committee may grant performance share awards to participants that entitle the recipient to receive share awards of common stock upon the achievement of certain performance goals and such other conditions as our compensation committee shall determine.

The compensation committee may grant cash bonuses under the 2014 Stock Option Plan to participants, subject to the achievement of certain performance goals.

The compensation committee may grant performance-based awards to participants in the form of restricted stock, restricted stock units, performance shares or cash-based awards upon the achievement of certain performance goals and such other conditions as the compensation committee shall determine. The compensation committee may grant such performance-based awards under the 2014 Stock Option Plan that are intended to qualify as “performance-based compensation” under Section 162(m) of the Code. Those awards would only vest or become payable upon the attainment of performance goals that are established by our compensation committee and related to one or more performance criteria. The performance criteria that could be used with respect to any such awards include: total shareholder return, earnings before interest, taxes, depreciation and amortization, net income (loss) (either before or after interest, taxes, depreciation and/or amortization), changes in the market price of our common stock, economic value-added, sales or revenue, development, clinical or regulatory milestones, acquisitions or strategic transactions, operating income (loss), cash flow (including, but not limited to, operating cash flow and free cash flow), return on capital, assets, equity, or investment, return on sales, gross or net profit levels, productivity, expense, margins, operating efficiency, customer satisfaction, working capital, earnings (loss) per share of stock, sales or market shares and number of customers, any of which may be measured either in absolute terms or as compared to any incremental increase or as compared to results of a peer group. From and after the time that we become subject to Section 162(m) of the Code, the maximum award that is intended to qualify as “performance-based compensation” under Section 162(m) of the Code that may be made to any one employee during any one calendar year period is \_\_\_\_\_ shares with respect to a stock-based award and \$ \_\_\_\_\_ with respect to a cash-based award.

The 2014 Stock Option Plan provides that upon the effectiveness of a “sale event,” as defined in the 2014 Stock Option Plan, all options and stock appreciation rights that are not exercisable immediately prior to the

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effective time of the sale event shall become fully exercisable as of the effective time of the sale event, all other awards with time-based vesting, conditions or restrictions, shall become fully vested and nonforfeitable as of the effective time of the sale event and all awards with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in the discretion of the compensation committee and all awards granted under the 2014 Stock Option Plan shall terminate. In addition, in connection with the termination of the 2014 Stock Option Plan upon a sale event, we may make or provide for a cash payment to participants holding options and stock appreciation rights equal to the difference between the per share cash consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights.

Our board of directors may amend or discontinue the 2014 Stock Option Plan and our compensation committee may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose, including option repricing, but no such action may adversely affect rights under an award without the holder's consent. Certain amendments to the 2014 Stock Option Plan may require the approval of our stockholders.

No awards may be granted under the 2014 Stock Option Plan after the date that is ten years from the date of stockholder approval of the 2014 Stock Option Plan.

### **Senior Executive Cash Incentive Bonus Plan**

On \_\_\_\_\_, 2014, our board of directors adopted the Senior Executive Cash Incentive Bonus Plan, or the Bonus Plan, which will become effective upon completion of this offering. The Bonus Plan provides for cash bonus payments based upon the attainment of performance targets established by our compensation committee. The payment targets will be related to corporate, financial and operational measures or objectives, or Corporate Performance Goals, as well as individual performance objectives.

Our compensation committee may select Corporate Performance Goals from among the following: cash flow (including, but not limited to, operating cash flow and free cash flow); sales or revenue; corporate revenue; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of our common stock; economic value-added; development, clinical or regulatory milestones; acquisitions or strategic transactions; operating income (loss); return on capital, assets, equity, or investment; stockholder returns; return on sales; gross or net profit levels; productivity; expense efficiency; margins; operating efficiency; customer satisfaction; working capital; earnings (loss) per share of our common stock; bookings, new bookings or renewals; sales or market shares; number of customers; number of new customers or customer references; operating income and/or net annual recurring revenue, any of which may be measured in absolute terms, as compared to any incremental increase, in terms of growth, as compared to results of a peer group, against the market as a whole, compared to applicable market indices and/or measured on a pre-tax or post-tax basis.

Each executive officer who is selected to participate in the Bonus Plan will have a target bonus opportunity set for each performance period. The bonus formulas will be adopted in each performance period by the compensation committee and communicated to each executive. The Corporate Performance Goals will be measured at the end of each performance period after our financial reports have been published or such other appropriate time as the compensation committee determines. If the Corporate Performance Goals and individual performance objectives are met, payments will be made as soon as practicable following the end of each performance period. Subject to the rights contained in any agreement between the executive officer and the company, an executive officer must be employed by the company on the bonus payment date to be eligible to receive a bonus payment. The Bonus Plan also permits the compensation committee to approve additional bonuses to executive officers in its sole discretion.

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**Simple IRA**

In 2009, we established a Savings Incentive Match Plan for employees. Under the terms of the plan, we contribute 2% of an employee's annual base salary, up to a maximum of the annual Internal Revenue Service compensation limits, for all full-time employees.

**Other Compensation**

We currently maintain broad-based benefits that are provided to all employees, including health insurance, life and disability insurance and dental insurance.



## CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than compensation arrangements, we describe below the transactions, and series of similar transactions, since January 1, 2011, to which we were a party or will be a party, in which:

- the amounts involved exceeded or will exceed \$120,000; and
- any of our directors, executive officers or holders of more than 5% of our capital stock, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

In connection with this offering, we plan to adopt a written policy, effective upon completion of this offering, that requires all future transactions between us and any director, executive officer, holder of 5% or more of any class of our capital stock or any member of the immediate family of, or entities affiliated with, any of them, or any other related persons (as defined in Item 404 of Regulation S-K) or their affiliates, in which the amount involved is equal to or greater than \$120,000, be approved in advance by our audit committee. Any request for such a transaction must first be presented to our audit committee for review, consideration and approval. In approving or rejecting any such proposal, our audit committee is to consider the relevant facts and circumstances available and deemed relevant to the audit committee, including, but not limited to, the extent of the related party's interest in the transaction, and whether the transaction is on terms no less favorable to us than terms we could have generally obtained from an unaffiliated third party under the same or similar circumstances.

All of the transactions described below were entered into prior to the adoption of this written policy but each was approved by our board of directors. Prior to our board of directors' consideration of a transaction with a related person, the material facts as to the related person's relationship or interest in the transaction were disclosed to our board of directors, and the transaction was not approved by our board of directors unless a majority of the directors approved the transaction. Our current policy with respect to approval of related person transactions is not set forth in writing.

### Private Placements of Securities

#### *Series C Financing*

On June 30, 2011, we entered into a securities purchase agreement, as amended, with TRV, Atlas and certain other existing investors of the company pursuant to which we issued, in a series of closings, an aggregate of 16,732,284 shares of our Series C redeemable convertible preferred stock at a price of \$0.90610 per share.

The following table summarizes the participation in the Series C redeemable convertible preferred stock financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons.

Name	Shares of Series C	Aggregate	Date Purchased
	Preferred	Purchase Price Paid	
Atlas Venture Fund VII, L.P.	3,310,892	\$ 2,999,999	6/30/2011
Atlas Venture Fund VII, L.P.	1,103,630	\$ 999,999	12/1/2011
Atlas Venture Fund VII, L.P.	3,849,073	\$ 3,487,645	2/1/2012
Third Rock Ventures, L.P.	3,310,892	\$ 2,999,999	6/30/2011
Third Rock Ventures, L.P.	1,103,630	\$ 999,999	12/1/2011
Third Rock Ventures, L.P.	3,849,073	\$ 3,487,645	2/1/2012

#### *August 2012 Convertible Note Financing*

On August 13, 2012, we entered into a note purchase agreement pursuant to which we issued promissory notes, in two closings, for an aggregate principal amount of \$6,000,000 to TRV and Atlas, which were convertible, under certain circumstances, into shares of the company's stock issued in the next qualified financing round. The promissory notes incurred interest at a rate of 8% per annum.

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The following table summarizes the participation in the convertible promissory note financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons.

<u>Name</u>	<u>Convertible Promissory Note Principal Amount</u>	<u>Date Purchased</u>
Atlas Venture Fund VII, L.P.	\$ 1,500,000	8/13/2012
Atlas Venture Fund VII, L.P.	\$ 1,500,000	11/8/2012
Third Rock Ventures, L.P.	\$ 1,500,000	8/13/2012
Third Rock Ventures, L.P.	\$ 1,500,000	11/8/2012

On November 30, 2012, the principal and accrued interest of these convertible promissory notes were converted, in accordance with their terms and at their respective conversion prices, into shares of Series D redeemable convertible preferred stock, and following such conversion, the notes were cancelled.

### *Series D Financing*

On November 30, 2012, we entered into a securities purchase agreement with TRV, Atlas and certain other investors pursuant to which we agreed to issue, in a series of closings, up to an aggregate of 16,011,162 shares of our Series D redeemable convertible preferred stock at a price of \$1.3592 per share for shares purchased for cash and \$1.22328 for shares issued upon conversion of convertible promissory notes and interest accrued thereon.

The following table summarizes the participation in the Series D redeemable convertible preferred stock financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons.

<u>Name</u>	<u>Shares of Series D Preferred</u>	<u>Aggregate Purchase Price Paid</u>	<u>Date Purchased</u>
Atlas Venture Fund VII, L.P.	2,487,630	\$ 3,043,068	11/30/2012
Atlas Venture Fund VII, L.P.	2,203,066	\$ 2,994,407	1/11/2013
Third Rock Ventures, L.P.	2,487,630	\$ 3,043,068	11/30/2012
Third Rock Ventures, L.P.	2,178,848	\$ 2,961,491	1/11/2013
Alta Partners VIII, L.P.	6,621,542	\$ 9,000,000	11/30/2012

### *Series E Financing*

On November 25, 2013, we entered into a securities purchase agreement with TRV, Atlas, Alta, Fidelity, and certain other investors pursuant to which we agreed to issue, in a series of closings, up to an aggregate of 20,919,679 shares of our Series E redeemable convertible preferred stock at a price of \$2.1725 per share.

The following table summarizes the participation in the Series E redeemable convertible preferred stock financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons.

<u>Name</u>	<u>Shares of Series E Preferred</u>	<u>Aggregate Purchase Price Paid</u>	<u>Date Purchased</u>
Alta Partners VIII, L.P.	690,449	\$ 1,500,000	11/25/2013
Entities Affiliated with Fidelity Investment	5,983,890	\$ 13,000,000	11/25/2013

### **Agreements with Stockholders**

In connection with the Series E redeemable convertible preferred stock financing, we entered into the Third Amended and Restated Investors' Rights Agreement, or investor rights agreement, dated as of November 25, 2013, with certain of our stockholders, including our principal stockholders and their affiliates, the Third

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Amended and Restated Voting Agreement, dated as of November 25, 2013, with certain of our stockholders, including our principal stockholders and their affiliates, and the Third Amended and Restated Right of First Refusal and Co-Sale Agreement, dated as of November 25, 2013, with certain of our stockholders, including our principal stockholders and their affiliates. All of the provisions of these agreements will terminate immediately upon completion of the offering, other than the provisions relating to registration rights, which will continue in effect following completion of the offering and entitle the holders of such rights to have us register their shares of our common stock for sale in the United States. See “Description of Capital Stock—Registration Rights.”

### **Executive Officer and Director Compensation**

See “Executive and Director Compensation” for information regarding compensation of directors and executive officers.

### **Employment Agreements**

We have entered into offer letters or employment agreements with our executive officers. For more information regarding our agreements with our named executive officers for the fiscal year ended 2013, see “Executive and Director Compensation—Narrative to Summary Compensation Table—Employment Arrangements with Our Named Executive Officers.”

### **Indemnification Agreements**

We have entered into or plan to enter into indemnification agreements with each of our directors and officers, the form of which is attached as an exhibit to the registration statement of which this prospectus is a part. The indemnification agreements and our amended and restated certificate of incorporation and amended and restated by-laws require us to indemnify our directors and officers to the fullest extent permitted by Delaware law.

**PRINCIPAL STOCKHOLDERS**

The following table presents information concerning the beneficial ownership of the shares of our common stock as of February 28, 2014 by:

- each person we know to be the beneficial owner of 5% or more of our outstanding shares of our capital stock;
- each of our directors;
- each of our named executive officers; and
- all of our executive officers and directors as a group.

We have determined beneficial ownership in accordance with SEC rules. The information does not necessarily indicate beneficial ownership for any other purpose. Under these rules, a person is deemed to be a beneficial owner of our common stock if that person has a right to acquire ownership within 60 days by the exercise of vested options or the conversion of our redeemable convertible preferred stock. A person is also deemed to be a beneficial holder of our common stock if that person has or shares voting power, which includes the power to vote or direct the voting of our common stock, or investment power, which includes the power to dispose of or to direct the disposition of such capital stock. Except in cases where community property laws apply or as indicated in the footnotes to this table, we believe that each stockholder identified in the table possesses sole voting and investment power over all shares of common stock shown as beneficially owned by the stockholder.

Percentage of beneficial ownership in the table below is based on 99,268,174 shares of common stock deemed to be outstanding as of February 28, 2014, assuming the conversion of all outstanding shares of redeemable convertible preferred stock into common stock, and \_\_\_\_\_ shares of common stock outstanding after the completion of this offering. The table below assumes that the underwriters do not exercise their over-allotment option. If the over-allotment option is exercised in full, we will sell an aggregate of \_\_\_\_\_ additional shares of common stock. Shares of common stock subject to options that are currently exercisable or exercisable within 60 days of February 28, 2014 are considered outstanding and beneficially owned by the person holding the options for the purpose of computing the percentage ownership of that person but are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless indicated below, the address of each individual listed below is c/o Zafgen, Inc., One Broadway, 8<sup>th</sup> Floor, Cambridge, MA 02142.

Name and address of beneficial owner <sup>(1)</sup>	Shares beneficially owned prior to offering		Shares beneficially owned after the offering	
	Number	Percent	Number	Percent
<b>5% Stockholders</b>				
Atlas Venture Fund VII, L.P. <sup>(2)</sup>	35,373,545	35.6%		
Third Rock Ventures, L.P. <sup>(3)</sup>	35,180,843	35.4%		
Alta Partners VIII, L.P. <sup>(4)</sup>	7,311,991	7.4%		
Entities Affiliated with Fidelity Investment <sup>(5)</sup>	5,983,890	6.0%		
<b>Named Executive Officers and Directors</b>				
Thomas E. Hughes, Ph.D. <sup>(6)</sup>	2,663,456	2.6%		
<b>Named Executive Officers</b>				
Dennis D. Kim, M.D., M.B.A. <sup>(7)</sup>	682,143	*		
Patricia L. Allen <sup>(8)</sup>	250,000	*		
<b>Other Directors</b>				
Peter Barrett, Ph.D. <sup>(9)</sup>	35,373,545	35.6%		
Bruce Booth, Ph.D. <sup>(10)</sup>	35,373,545	35.6%		
Avi Goldberg <sup>(11)</sup>	2,183,194	2.2%		
Kevin P. Starr <sup>(12)</sup>	50,921	*		
Lou Tartaglia, Ph.D. <sup>(13)</sup>	—	—		
<b>All directors and executive officers as a group (8 persons)<sup>(14)</sup></b>	<b>41,203,259</b>	<b>40.1%</b>		

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\* Indicates beneficial ownership of less than one percent.

- (1) Unless otherwise indicated, the address for each beneficial owner is c/o Zafgen, Inc., One Broadway, 8th Floor, Cambridge, Massachusetts 02142.
- (2) The address for Atlas Venture Fund VII, L.P., or Atlas Venture VII, is 25 First Street, Suite 303, Cambridge, MA 02141. Consists of (i) 4,768,001 shares of common stock issuable upon conversion of shares of Series A redeemable convertible preferred stock, (ii) 17,651,253 shares of common stock issuable upon conversion of shares of Series B redeemable convertible preferred stock, (iii) 8,263,595 shares of common stock issuable upon conversion of shares of Series C redeemable convertible preferred stock and (iv) 4,690,696 shares of common stock issuable upon conversion of shares of Series D redeemable convertible preferred stock. All shares are held directly by Atlas Venture VII. Atlas Venture Associates VII, L.P., or AVA VII LP, is the general partner of Atlas Venture VII, and Atlas Venture Associates VII, Inc., or AVA VII Inc., is the general partner of AVA VII LP. Peter Barrett, Bruce Booth, Jean-Francois Formela and Jeff Fagnan is each a director of AVA VII Inc. Drs. Booth and Barrett are members of our board of directors. Each of the reporting persons disclaims beneficial ownership of such shares, except to the extent of their proportionate pecuniary interest therein, if any.
- (3) The address for Third Rock Ventures, L.P., or TRV LP, is 29 Newbury Street, 3rd Floor, Boston, MA 02116. Consists of (i) 22,250,770 shares of common stock issuable upon conversion of shares of Series B redeemable convertible preferred stock, (ii) 8,263,595 shares of common stock issuable upon conversion of shares of Series C redeemable convertible preferred stock and (iii) 4,666,478 shares of common stock issuable upon conversion of shares of Series D redeemable convertible preferred stock. All shares are held directly by TRV LP. Each of Third Rock Ventures GP, LP, or TRV GP, the general partner of TRV LP, and Third Rock Ventures GP, LLC, or TRV LLC, the general partner of TRV GP, may be deemed to have voting and dispositive power over the shares held by TRV LP. Investment decisions with respect to the shares held by TRV LP are made by an investment committee at TRV GP comprised of Mark Levin, Kevin Starr, Bob Tepper, Neil Exter, Kevin Gillis, Lou Tartaglia, Craig Muir, Cary Pfeffer, Alexis Borisy and Craig Greaves. No stockholder, director, officer, manager, member or employee of TRV GP or TRV LLC has beneficial ownership (within the meaning of Rule 13d-3 promulgated under the Exchange Act) of any shares held by TRV LP. Dr. Tartaglia and Mr. Starr are members of our board of directors.
- (4) The address for Alta Partners VIII, L.P. is One Embarcadero Center, 37th Floor, San Francisco, CA 94111. Consists of (i) 6,621,542 shares of common stock issuable upon conversion of shares of Series D redeemable convertible preferred stock and (ii) 690,449 shares of common stock issuable upon conversion of shares of Series E redeemable convertible preferred stock. These shares are held of record by Alta Partners VIII, L.P. Alta Partners Management VIII, LLC is the general partner of Alta Partners VIII, L.P. Guy Nohra, Daniel Janney and Farah Champsi are managing directors of Alta Partners Management VIII, LLC and exercise shared voting and investment powers with respect to the shares owned by Alta Partners VIII, L.P. Each of the reporting persons disclaims beneficial ownership of such shares, except to the extent of their proportionate pecuniary interest therein, if any.
- (5) Fidelity Management & Research Company, or Fidelity, 82 Devonshire Street, Boston, Massachusetts 02109, a wholly-owned subsidiary of FMR LLC and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of shares of common stock as a result of acting as investment adviser to various investment companies registered under Section 8 of the Investment Company Act of 1940. Consists of (i) 5,172,990 shares of common stock issuable upon conversion of shares of Series E redeemable convertible preferred stock held by Fidelity Select Portfolios: Biotech Portfolio, and (ii) 810,900 shares of common stock issuable upon conversion of shares of Series E redeemable convertible preferred stock held by Fidelity Advisor Series VII: Fidelity Advisor Biotech Fund. Edward C. Johnson 3d and FMR LLC, through its control of Fidelity, and the funds each has sole power to dispose of the shares owned by the Funds. Members of the family of Edward C. Johnson 3d, Chairman of FMR LLC, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting

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common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d, Chairman of FMR LLC, has the sole power to vote or direct the voting of the shares owned directly by the Fidelity Funds, which power resides with the Funds' Boards of Trustees. Fidelity carries out the voting of the shares under written guidelines established by the Funds' Boards of Trustees.

- (6) Consists of 221,396 shares of common stock and 2,442,060 shares of common stock issuable upon exercise of options within 60 days of February 28, 2014.
- (7) Consists of 682,143 shares of common stock issuable upon exercise of options within 60 days of February 28, 2014.
- (8) Consists of 250,000 shares of common stock issuable upon exercise of options within 60 days of February 28, 2014.
- (9) Consists of the shares described in note (2) above. Dr. Barrett is a general partner of Atlas Venture Fund VII, L.P., and as such Dr. Barrett may be deemed to share voting and dispositive power with respect to all shares held by such entity. Dr. Barrett disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Barrett's business address is 25 First Street, Suite 303, Cambridge, MA 02141.
- (10) Consists of the shares described in note (2) above. Dr. Booth is a general partner of Atlas Venture Fund VII, L.P., and as such Dr. Booth may be deemed to share voting and dispositive power with respect to all shares held by such entity. Dr. Booth disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Booth's business address is 25 First Street, Suite 303, Cambridge, MA 02141.
- (11) Consists of 2,183,194 shares of common stock held by Greatpoint Ventures Fund I, LLC, or GPV. Mr. Goldberg is a partner at GPV and as such Mr. Goldberg may be deemed to share voting and dispositive power with respect to all shares held by GPV. Mr. Goldberg disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Mr. Goldberg's business address is 71 Summer Street, 4th floor, Boston, MA 02110.
- (12) Consists of 50,921 shares of common stock Mr. Starr holds in his individual capacity. Investment decisions with respect to the shares held by TRV LP are made by an investment committee at TRV GP comprised of Mark Levin, Kevin Starr, Bob Tepper, Neil Exter, Kevin Gillis, Lou Tartaglia, Craig Muir, Cary Pfeffer, Alexis Borisy and Craig Greaves. No stockholder, director, officer, manager, member or employee of TRV GP or TRV LLC has beneficial ownership (within the meaning of Rule 13d-3 promulgated under the Exchange Act) of any shares held by TRV LP.
- (13) Investment decisions with respect to the shares held by TRV LP are made by an investment committee at TRV GP comprised of Mark Levin, Kevin Starr, Bob Tepper, Neil Exter, Kevin Gillis, Lou Tartaglia, Craig Muir, Cary Pfeffer, Alexis Borisy and Craig Greaves. No stockholder, director, officer, manager, member or employee of TRV GP or TRV LLC has beneficial ownership (within the meaning of Rule 13d-3 promulgated under the Exchange Act) of any shares held by TRV LP.
- (14) Includes 3,117,816 shares of common stock issuable upon exercise of options within 60 days of December 1, 2013.

## DESCRIPTION OF CAPITAL STOCK

Upon the completion of this offering, our authorized capital stock will consist of \_\_\_\_\_ shares of common stock, par value \$0.001 per share, and \_\_\_\_\_ shares of preferred stock, par value \$0.001 per share, all of which will be undesignated, and there will be \_\_\_\_\_ shares of common stock outstanding and no shares of preferred stock outstanding. As of February 28, 2014, we had approximately \_\_\_\_\_ record holders of our capital stock. All of our outstanding shares of redeemable convertible preferred stock will automatically convert into shares of our common stock upon the completion of this offering. In addition, upon completion of this offering, \_\_\_\_\_ options to purchase shares of our common stock will be outstanding and \_\_\_\_\_ shares of our common stock will be reserved for future grants under our stock option plans.

The following description of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated by-laws are summaries of material terms and provisions and are qualified by reference to our amended and restated certificate of incorporation and amended and restated by-laws, copies of which have been filed with the SEC as exhibits to the registration statement of which this prospectus is a part. The descriptions of our common stock and preferred stock reflect amendments to our amended and restated certificate of incorporation and amended and restated by-laws that will become effective immediately prior to the completion of this offering.

### Common Stock

Upon the completion of this offering, we will be authorized to issue one class of common stock. Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Except as described under “Antitakeover Effects of Delaware Law and Provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated By-laws” below, a majority vote of the holders of common stock is generally required to take action under our amended and restated certificate of incorporation and amended and restated by-laws.

### Preferred Stock

Upon the completion of this offering, our board of directors will be authorized, without action by the stockholders, to designate and issue up to an aggregate of \_\_\_\_\_ shares of preferred stock in one or more series. Our board of directors can designate the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes could, under certain circumstances, have the effect of restricting dividends on our common stock, diluting the voting power of our common stock, impairing the liquidation rights of our common stock, or delaying, deferring or preventing a change in control of our company, which might harm the market price of our common stock. See also “Antitakeover Effects of Delaware Law and Provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated By-laws—Provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated By-laws—Undesignated preferred stock” below.

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Our board of directors will make any determination to issue such shares based on its judgment as to our company's best interests and the best interests of our stockholders. Upon the completion of this offering, we will have no shares of preferred stock outstanding and we have no current plans to issue any shares of preferred stock following completion of this offering.

### **Registration Rights**

Upon the completion of this offering, the holders of 95,029,181 shares of our common stock, including shares issuable upon the conversion of our redeemable convertible preferred stock or their permitted transferees, are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of an investor rights agreement between us and the holders of our redeemable convertible preferred stock. The investor rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under the investor rights agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

#### *Demand Registration Rights*

Upon the completion of this offering, the holders of 95,029,181 shares of our common stock, including shares issuable upon the conversion of our redeemable convertible preferred stock or their permitted transferees, are entitled to demand registration rights. Under the terms of the investor rights agreement, we will be required, upon the written request of holders of 70% of these securities, to use our best efforts to file a registration statement and use reasonable, diligent efforts to affect the registration of all or a portion of these shares for public resale. We are required to effect only one registration pursuant to this provision of the investor rights agreement. A demand for registration may not be made until 180 days after the completion of this offering.

#### *Short Form Registration Rights*

Upon the completion of this offering, the holders of 95,029,181 shares of our common stock, including shares issuable upon the conversion of our redeemable convertible preferred stock or their permitted transferees, are also entitled to short form registration rights. Pursuant to the investor rights agreement, if we are eligible to file a registration statement on Form S-3, upon the request of 10% of these holders to sell registrable securities at an aggregate price of at least \$500,000, we will be required to use our best efforts to affect a registration of such shares. We are required to effect only one registration in any twelve month period pursuant to this provision of the investor rights agreement.

#### *Piggyback Registration Rights*

The holders of 95,029,181 shares of our common stock, including shares issuable upon the conversion of our redeemable convertible preferred stock or their permitted transferees, are entitled to piggyback registration rights. If we register any of our securities either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions contained in the investor rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering if the underwriters determine in good faith that marketing factors require a limitation of the number of shares to be underwritten.

#### *Indemnification*

Our investor rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.



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### *Expiration of Registration Rights*

The registration rights granted under the investor rights agreement will terminate upon the earlier of (i) a deemed liquidation event, as defined in our amended and restated certificate of incorporation or (ii) at such time when all registrable securities could be sold without restriction under Rule 144 of the Securities Act.

### **Antitakeover Effects of Delaware Law and Provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated By-laws**

Certain provisions of the Delaware General Corporation Law and of our amended and restated certificate of incorporation and amended and restated by-laws that will become effective upon the completion of this offering could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our board of directors. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

### *Delaware Takeover Statute*

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

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- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

### *Provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated By-laws*

Our amended and restated certificate of incorporation and amended and restated by-laws to be in effect upon completion of this offering will include a number of provisions that may have the effect of delaying, deferring or discouraging another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

*Board composition and filling vacancies.* In accordance with our amended and restated certificate of incorporation, our board is divided into three classes serving staggered three-year terms, with one class being elected each year. Our amended and restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum.

*No written consent of stockholders.* Our amended and restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our by-laws or removal of directors by our stockholder without holding a meeting of stockholders.

*Meetings of stockholders.* Our amended and restated by-laws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our amended and restated by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

*Advance notice requirements.* Our amended and restated by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in our amended and restated by-laws.

*Amendment to certificate of incorporation and by-laws.* As required by the Delaware General Corporation Law, any amendment of our amended and restated certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our amended and restated certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that

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the amendment of the provisions relating to stockholder action, directors, limitation of liability and the amendment of our amended and restated certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our amended and restated by-laws may be amended by the affirmative vote of a majority vote of the directors then in office, subject to any limitations set forth in the amended and restated by-laws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

*Undesignated preferred stock.* Our amended and restated certificate of incorporation provides for authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our amended and restated certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

### **Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is . The transfer agent and registrar's address is .

### **Listing**

We have applied to list our common stock on the NASDAQ Global Market under the symbol "ZFGN."

## SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Based on the number of shares of common stock outstanding as of February 28, 2014, upon completion of this offering, \_\_\_\_\_ shares of common stock will be outstanding, assuming no exercise of the underwriter's over-allotment option and no exercise of options. All of the shares sold in this offering will be freely tradable. The remaining shares of common stock outstanding after this offering will be restricted as a result of securities laws or lock-up agreements as described below. Following the expiration of the lock-up period, all shares will be eligible for resale in compliance with Rule 144 or Rule 701 under the Securities Act. "Restricted securities" as defined under Rule 144 of the Securities Act were issued and sold by us in reliance on exemptions from the registration requirements of the Securities Act. These shares may be sold in the public market only if registered or qualified for an exemption from registration, such as under Rule 144 or Rule 701 under the Securities Act.

### Rule 144

In general, under Rule 144 under the Securities Act of 1933, as in effect on the date of this prospectus, a person who is one of our affiliates and has beneficially owned shares of our common stock for at least six months would be entitled to sell within any three-month period a number of shares that does not exceed the greater of:

- one percent of the number of shares of common stock then outstanding, which will equal approximately \_\_\_\_\_ shares immediately after the completion of this offering; or
- the average weekly trading volume of our common stock on the NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Sales under Rule 144 by our affiliates or persons selling shares on behalf of our affiliates are also subject to manner of sale provisions and notice requirements and to the availability of current public information about us. For a person who has not been deemed to have been one of our affiliates at any time during the 90 days preceding a sale, sales of our securities held longer than six months, but less than one year, will be subject only to the current public information requirement.

In general, under Rule 144 under the Securities Act, as in effect on the date of this prospectus, a person who is not deemed to have been one of our affiliates at any time during the 90 days preceding a sale, and who has beneficially owned the shares proposed to be sold for at least six months, including the holding period of any prior owner other than an affiliate, is entitled to sell the shares without complying with the manner of sale, volume limitation or notice provisions of Rule 144, and will be subject only to the public information requirements of Rule 144. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than our affiliates, then such person is entitled to sell such shares without complying with any of the requirements of Rule 144. \_\_\_\_\_ shares of our common stock will qualify for resale under Rule 144 within 180 days of the date of this prospectus, subject to the lock-up agreements as described under "Lock-up Agreements" below and under "Underwriting" in this prospectus, and to the extent such shares have been released from any repurchase option that we may hold.

### Rule 701

Rule 701 under the Securities Act, or Rule 701, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the

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holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and under “Underwriting” included elsewhere in this prospectus and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

### **Lock-up Agreements**

In connection with this offering, we, each of our directors and executive officers, and holders holding \_\_\_\_\_ shares of our outstanding stock have agreed that, subject to limited exceptions, which include:

- sales of securities acquired in open market transactions after the completion of this offering,
- transfers of securities (i) as a bona fide gift or gifts or (ii) by will or intestacy to the legal representative, heir, beneficiary or a member of the immediate family of the undersigned in a transaction not involving a disposition for value,
- if the holder is an individual, transfers of shares of our common stock or any security convertible into our common stock to any trust for the benefit of the holder or the immediate family of the undersigned, or limited partnerships the partners of which are the holder and/or the immediate family members of the holder, in each case for estate planning purposes,
- if the holder is a trust, distributions of shares of our common stock or any security convertible into our common stock to its beneficiaries in a transaction not involving a disposition for value,
- if the holder is a corporation, limited liability company, partnership or other entity, distribution of shares of our common stock or any security convertible into our common stock to members, stockholders, limited partners, subsidiaries or affiliates (as defined in Rule 405 promulgated under the Securities Act of 1933, as amended) of the holder or to any investment fund or other entity that controls or manages the holder in a transaction not involving a disposition for value,
- the receipt by the holder of shares of our common stock in connection with the conversion of our outstanding preferred stock into shares of our common stock,
- transfers to us pursuant to agreements under which we have the option to repurchase such shares or securities upon termination of service of the holder,
- the receipt by the holder from us of shares of our common stock upon the exercise of options, and
- the establishment of a trading plan that satisfies the requirements of Rule 10b5-1 under the Exchange Act for the transfer of shares of our common stock,

without the prior written consent of Leerink Partners LLC and Cowen and Company, LLC on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into, or exercisable or exchangeable for, our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) or publicly disclose the intention to make any offer, sale, pledge or disposition, (2) enter into any swap or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock or such other securities, whether any such transaction is to be settled by delivery of our common stock or such other securities, in cash or otherwise or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock.

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**Registration Rights**

We are party to an investor rights agreement which provides that holders holding \_\_\_\_\_ shares of our redeemable convertible preferred stock have the right to demand that we file a registration statement or request that their shares of our common stock be covered by a registration statement that we are otherwise filing. See “Description of Capital Stock—Registration Rights” in this prospectus. Except for shares purchased by affiliates, registration of their shares under the Securities Act would result in these shares becoming freely tradable without restriction under the Securities Act immediately upon effectiveness of the registration, subject to the expiration of the lock-up period described above and under “Underwriting” in this prospectus, and to the extent such shares have been released from any repurchase option that we may hold.

**Stock Option Plan**

As soon as practicable after the completion of this offering, we intend to file a Form S-8 registration statement under the Securities Act to register shares of our common stock subject to options outstanding or reserved for issuance under our stock plans. This registration statement will become effective immediately upon filing, and shares covered by this registration statement will thereupon be eligible for sale in the public markets, subject to Rule 144 limitations applicable to affiliates and any lock-up agreements. For a more complete discussion of our stock plans, see “Executive and Director Compensation—Stock Option Plans.”

**MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS TO  
NON-U.S. HOLDERS**

The following is a general discussion of certain material U.S. federal income and estate tax considerations relating to ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term “non-U.S. holder” means a beneficial owner of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or of any political subdivision of the United States;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons (as defined in the Code) have authority to control all substantial decisions of the trust or if the trust has a valid election in effect to be treated as a U.S. person under applicable U.S. Treasury Regulations.

A modified definition of “non-U.S. holder” applies for U.S. federal estate tax purposes (as discussed below).

This discussion is based on current provisions of the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. In addition, the Internal Revenue Service, or the IRS, could challenge one or more of the tax consequences described in this prospectus.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment) within the meaning of Section 1221 of the Code. This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder’s individual circumstances nor does it address any aspects of state, local or non-U.S. taxes, or U.S. federal taxes other than income and estate taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;
- controlled foreign corporations;
- passive foreign investment companies;
- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- certain U.S. expatriates;
- persons who have elected to mark securities to market;

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- persons subject to the unearned income Medicare contribution tax;
- persons subject to the alternative minimum tax; or
- persons that acquire our common stock as compensation for services.

In addition, this discussion does not address the tax treatment of partnerships (including any entity or arrangement treated as a partnership for U.S. federal income tax purposes) or other entities that are transparent for U.S. federal income tax purposes or persons who hold their common stock through partnerships or other entities that are transparent for U.S. federal income tax purposes. In the case of a holder that is classified as a partnership for U.S. federal income tax purposes, the tax treatment of a person treated as a partner in such partnership for U.S. federal income tax purposes generally will depend on the status of the partner and the activities of the partner and the partnership. A person treated as a partner in a partnership or who holds their stock through another transparent entity should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other transparent entity, as applicable.

Prospective investors should consult their own tax advisors regarding the U.S. federal, state, local and non-U.S. income and other tax considerations of acquiring, holding and disposing of our common stock.

### **Distributions on our Common Stock**

We do not currently expect to pay dividends. See “Dividend Policy” above in this prospectus. However, in the event that we do pay distributions of cash or property on our common stock (or in the case of certain redemptions that are treated as distributions with respect to our common stock), those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder’s investment, up to such holder’s tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading “Gain on Sale, Exchange or Other Taxable Disposition of Common Stock.”

Subject also to the discussions below under the headings “Information Reporting and Backup Withholding Tax” and “Foreign Account Tax Compliance Act,” dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence. If we determine, at a time reasonably close to the date of payment of a distribution on our common stock, that the distribution will not constitute a dividend because we do not anticipate having current or accumulated earnings and profits, we intend not to withhold any U.S. federal income tax on the distribution as permitted by U.S. Treasury Regulations. If we or another withholding agent apply over-withholding, a non-U.S. holder may be entitled to a refund or credit of any excess tax withheld by timely filing an appropriate claim with the IRS.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. To obtain this exemption, a non-U.S. holder must generally provide us with a properly executed original and unexpired IRS Form W-8ECI properly certifying such exemption. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional “branch profits tax” at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence.



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A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Any documentation provided to an applicable withholding agent may need to be updated in certain circumstances. The certification requirements described above also may require a non-U.S. holder to provide its U.S. taxpayer identification number.

### **Gain on Sale, Exchange or Other Taxable Disposition of Common Stock**

Subject to the discussions below under the headings "Information Reporting and Backup Withholding Tax" and "Foreign Account Tax Compliance Act," a non-U.S. holder generally will not be subject to U.S. federal income tax or withholding tax on gain recognized on a sale, exchange or other taxable disposition of our common stock (other than a redemption that is treated as a distribution for U.S. federal income tax purposes and taxed as described above) unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States, and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder will be taxed on a net income basis at the regular graduated rates and in the manner applicable to U.S. persons, and, if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a rate of 30%, or a lower rate as may be specified by an applicable income tax treaty, may also apply;
- the non-U.S. holder is an individual present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the amount by which the non-U.S. holder's capital gains allocable to U.S. sources exceed capital losses allocable to U.S. sources during the taxable year of the disposition ; or
- we are or were a "U.S. real property holding corporation" during a certain look-back period, unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than five percent of our outstanding common stock, directly or indirectly, during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a "U.S. real property holding corporation" if the fair market value of its "U.S. real property interests" equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we believe that we have not been and are not currently, and we do not anticipate becoming, a "U.S. real property holding corporation" for U.S. federal income tax purposes.

If these exceptions do not apply, gain on the disposition of shares of our common stock will generally be taxed in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax will not apply.

### **Information Reporting and Backup Withholding Tax**

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S.

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holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Generally, a holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Any documentation provided to an applicable withholding agent may need to be updated in certain circumstances.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

### **Foreign Account Tax Compliance Act**

Legislation commonly referred to as the Foreign Account Tax Compliance Act and associated guidance, or collectively, FATCA, will generally impose a 30% withholding tax on any "withholdable payment" (as defined below) to a "foreign financial institution," unless such institution enters into an agreement with the U.S. government to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which would include certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with United States owners) or another applicable exception applies or such institution is compliant with applicable foreign law enacted in connection with an applicable intergovernmental agreement between the United States and a foreign jurisdiction. FATCA will also generally impose a 30% withholding tax on any "withholdable payment" (as defined below) to a foreign entity that is not a financial institution, unless such entity provides the withholding agent with a certification identifying the substantial U.S. owners of the entity (which generally includes any U.S. person who directly or indirectly owns more than 10% of the entity), if any, or another applicable exception applies or such entity is compliant with applicable foreign law enacted in connection with an applicable intergovernmental agreement between the United States and a foreign jurisdiction. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes.

Under final regulations and other current guidance, "withholdable payments" will generally include dividends on our common stock paid on or after July 1, 2014 and the gross proceeds of a disposition of our common stock paid on or after January 1, 2017. The FATCA withholding tax will apply regardless of whether a payment would otherwise be exempt from or not subject to U.S. nonresident withholding tax (e.g., under the portfolio interest exemption or as capital gain). The IRS is authorized to provide, and has begun the process of providing, rules for coordinating the FATCA withholding regime with the existing nonresident withholding tax rules.

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**Federal Estate Tax**

Common stock owned or treated as owned by an individual who is a non-U.S. holder (as specially defined for U.S. federal estate tax purposes) at the time of death will be included in the individual's gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

**The preceding discussion of material U.S. federal tax considerations is for general information only. It is not tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.**

## UNDERWRITING

We are offering the shares of common stock described in this prospectus through a number of underwriters. Leerink Partners LLC and Cowen and Company, LLC are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of Shares
Leerink Partners LLC	
Cowen and Company, LLC	
Canaccord Genuity Inc.	
JMP Securities LLC	
<b>Total</b>	

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of \$ per share. Any such dealers may resell shares to certain other brokers or dealers at a discount of up to \$ per share from the initial public offering price. After the initial public offering of the shares, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this over-allotment option. If any shares are purchased with this over-allotment option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without over-allotment exercise	With full over-allotment exercise
Per Share	\$	\$
Total	\$	\$

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$ .

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to

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allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or file with the Securities and Exchange Commission a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences of ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of Leerink Partners LLC and Cowen and Company, LLC for a period of 180 days after the date of this prospectus, other than the shares of our common stock to be sold hereunder and any shares of our common stock issued upon the exercise of options granted under our existing stock-based compensation plans.

Our directors and executive officers, and certain of our significant shareholders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 180 days after the date of this prospectus, may not, without the prior written consent of Leerink Partners LLC and Cowen and Company, LLC, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into, or exercisable or exchangeable for, our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock. We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

We have applied to list our common stock on The NASDAQ Global Market under the symbol “ZFGN”.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be “covered” shorts, which are short positions in an amount not greater than the underwriters’ over-allotment option referred to above, or may be “naked” shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their over-allotment option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the over-allotment option. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

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The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the NASDAQ, in the over-the-counter market or otherwise.

Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters expect to consider a number of factors including:

- the information set forth in this prospectus and otherwise available to the representatives;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our common shares, or that the shares will trade in the public market at or above the initial public offering price.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

This document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the “Order”) or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”). The securities are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such securities will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a “Relevant Member State”), from and including the date on which the European Union Prospectus Directive (the “EU Prospectus Directive”) was implemented in that Relevant Member State (the “Relevant Implementation Date”) an offer of securities described in this prospectus may not be made to the

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public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the EU Prospectus Directive, except that, with effect from and including the Relevant Implementation Date, an offer of securities described in this prospectus may be made to the public in that Relevant Member State at any time:

- to any legal entity which is a qualified investor as defined under the EU Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the EU Prospectus Directive); or

in any other circumstances falling within Article 3(2) of the EU Prospectus Directive, provided that no such offer of securities described in this prospectus shall result in a requirement for the publication by us of a prospectus pursuant to Article 3 of the EU Prospectus Directive.

For the purposes of this provision, the expression an “offer of securities to the public” in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in that Member State by any measure implementing the EU Prospectus Directive in that Member State. The expression “EU Prospectus Directive” means Directive 2003/71/EC (and any amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State, and the expression “2010 PD Amending Directive” means Directive 2010/73/EU.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

## LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts and for the underwriters by Ropes & Gray LLP, Boston, Massachusetts.

## EXPERTS

The financial statements as of December 31, 2013 and 2012 and for each of the three years in the period ended December 31, 2013 and, cumulatively, for the period from November 22, 2005 (date of inception) to December 31, 2013 included in this prospectus have been so included in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

## WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act that registers the shares of our common stock to be sold in this offering. This prospectus does not contain all of the information set forth in the registration statement and the exhibits and schedules filed as part of the registration statement. For further information with respect to us and our common stock, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Statements contained in this prospectus concerning the contents of any contract or any other document are not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, we refer you to the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The reports and other information we file with the SEC can be read and copied at the SEC's Public Reference Room at 100 F Street, NE, Washington D.C. 20549. Copies of these materials can be obtained at prescribed rates from the Public Reference Section of the SEC at the principal offices of the SEC, 100 F Street, NE, Washington D.C. 20549. You may obtain information regarding the operation of the public reference room by calling 1(800) SEC-0330. The SEC also maintains a web site (<http://www.sec.gov>) that contains reports, proxy and information statements and other information regarding issuers like us that file electronically with the SEC.

Upon completion of this offering, we will become subject to the reporting and information requirements of the Exchange Act and, as a result, will file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information will be available for inspection and copying at the SEC's public reference room and the web site of the SEC referred to above.



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**Report of Independent Registered Public Accounting Firm**

To the Board of Directors and Stockholders of  
Zafgen, Inc.

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations and comprehensive loss, of redeemable convertible preferred stock and stockholders' deficit and of cash flows present fairly, in all material respects, the financial position of Zafgen, Inc. and its subsidiaries (a development stage company) at December 31, 2013 and 2012, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2013 and, cumulatively, for the period from November 22, 2005 (date of inception) to December 31, 2013 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States), which require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts  
March 14, 2014

**ZAFGEN, INC.**  
(A Development Stage Company)

**CONSOLIDATED BALANCE SHEETS**  
(In thousands, except share and per share data)

	<u>December 31,</u>		<u>Pro Forma</u>
	<u>2012</u>	<u>2013</u>	<u>December 31,</u> <u>2013</u> <u>(unaudited)</u>
<b>Assets</b>			
Current assets:			
Cash and cash equivalents	\$ 9,935	\$ 35,517	\$ 35,517
Prepaid expenses and other current assets	389	224	224
Tax incentive receivable	—	1,617	1,617
Total current assets	10,324	37,358	37,358
Tax incentive receivable	630	—	—
Property and equipment, net	32	37	37
Deferred offering costs	—	743	743
Total assets	<u>\$ 10,986</u>	<u>\$ 38,138</u>	<u>\$ 38,138</u>
<b>Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)</b>			
Current liabilities:			
Accounts payable	\$ 1,231	\$ 2,015	\$ 2,015
Accrued expenses	1,699	900	900
Total current liabilities	2,930	2,915	2,915
Total liabilities	2,930	2,915	2,915
Commitments and contingencies (Note 10)			
Redeemable convertible preferred stock (Series A, B, C, D and E), \$0.001 par value; 78,372,931 and 99,292,610 shares authorized at December 31, 2012 and 2013, respectively; 73,991,017 and 94,483,404 shares issued and outstanding at December 31, 2012 and 2013, respectively; aggregate liquidation preference of \$104,588 at December 31, 2013; no shares issued or outstanding pro forma at December 31, 2013 (unaudited)	62,785	103,797	—
Stockholders' equity (deficit):			
Common stock, \$0.001 par value; 100,000,000 and 115,000,000 shares authorized at December 2012 and 2013, respectively; 4,622,336 and 4,580,669 shares issued and outstanding at December 31, 2012 and 2013, respectively; 99,064,073 shares issued and outstanding pro forma at December 31, 2013 (unaudited)	5	5	99
Additional paid-in capital	146	328	104,031
Deficit accumulated during the development stage	(54,880)	(68,907)	(68,907)
Total stockholders' equity (deficit)	(54,729)	(68,574)	35,223
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	<u>\$ 10,986</u>	<u>\$ 38,138</u>	<u>\$ 38,138</u>

The accompanying notes are an integral part of these consolidated financial statements.

**ZAFGEN, INC.**  
**(A Development Stage Company)**  
**CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**  
**(In thousands, except share and per share data)**

	<u>Year Ended December 31,</u>			<u>Cumulative Period From Inception (November 22, 2005) to December 31, 2013</u>
	<u>2011</u>	<u>2012</u>	<u>2013</u>	
Revenue	\$ —	\$ —	\$ —	\$ —
Operating expenses:				
Research and development	11,403	11,544	9,561	54,290
General and administrative	1,751	2,247	4,219	14,309
Total operating expenses	<u>13,154</u>	<u>13,791</u>	<u>13,780</u>	<u>68,599</u>
Loss from operations	<u>(13,154)</u>	<u>(13,791)</u>	<u>(13,780)</u>	<u>(68,599)</u>
Other income (expense):				
Interest income	—	—	—	120
Interest expense	—	(97)	—	(106)
Foreign currency transaction gains (losses), net	(3)	8	(247)	(243)
Total other expense, net	<u>(3)</u>	<u>(89)</u>	<u>(247)</u>	<u>(229)</u>
Net loss and comprehensive loss	<u>(13,157)</u>	<u>(13,880)</u>	<u>(14,027)</u>	<u>(68,828)</u>
Accretion of redeemable convertible preferred stock to redemption value	<u>(53)</u>	<u>(67)</u>	<u>(213)</u>	<u>(554)</u>
Net loss attributable to common stockholders	<u>\$ (13,210)</u>	<u>\$ (13,947)</u>	<u>\$ (14,240)</u>	<u>\$ (69,382)</u>
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (3.05)</u>	<u>\$ (3.13)</u>	<u>\$ (3.11)</u>	
Weighted average common shares outstanding, basic and diluted	<u>4,326,581</u>	<u>4,456,778</u>	<u>4,578,127</u>	
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)			<u>\$ (0.17)</u>	
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)			<u>84,189,565</u>	

The accompanying notes are an integral part of these consolidated financial statements.

**ZAFGEN, INC.**  
(A Development Stage Company)

**CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT**

(In thousands, except share data)

	Series A, B, C, D and E Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Deficit Accumulated During the Development Stage	Total Stockholders' Deficit
	Shares	Amount	Shares	Par Value			
<b>Balances at Inception (November 22, 2005)</b>	—	\$ —	—	\$ —	\$ —	\$ —	\$ —
Issuance of common stock	—	—	4,073,596	4	—	—	4
Issuance of restricted common stock	—	—	1,195,736	2	32	—	34
Issuance of common stock upon exercise of stock options	—	—	223,130	—	2	—	2
Issuance of common stock for services rendered	—	—	74,541	—	—	—	—
Repurchase and retirement of common stock, at cost	—	—	(1,045,588)	(1)	—	—	(1)
Issuance of Series A redeemable convertible preferred stock, net of issuance costs of \$82	4,768,001	1,918	—	—	—	—	—
Conversion of promissory notes to Series A redeemable convertible preferred stock	595,238	175	—	—	—	—	—
Issuance of Series B redeemable convertible preferred stock, net of issuance costs of \$111	36,741,738	27,630	—	—	—	—	—
Conversion of promissory notes and accrued interest to Series B redeemable convertible preferred stock	842,497	509	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	160	—	160
Accretion of redeemable convertible preferred stock to redemption value	—	221	—	—	(142)	(79)	(221)
Net loss	—	—	—	—	—	(27,764)	(27,764)
<b>Balances at December 31, 2010</b>	42,947,474	30,453	4,521,415	5	52	(27,843)	(27,786)
Issuance of Series B redeemable convertible preferred stock, net of issuance costs of \$9	2,682,011	2,016	—	—	—	—	—
Issuance of Series C redeemable convertible preferred stock, net of issuance costs of \$33	8,923,884	8,053	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	80	—	80
Accretion of redeemable convertible preferred stock to redemption value	—	53	—	—	(53)	—	(53)
Net loss	—	—	—	—	—	(13,157)	(13,157)
<b>Balances at December 31, 2011</b>	54,553,369	40,575	4,521,415	5	79	(41,000)	(40,916)
Issuance of Series C redeemable convertible preferred stock, net of issuance costs of \$8	7,808,400	7,067	—	—	—	—	—
Issuance of Series D redeemable convertible preferred stock, net of issuance costs of \$54	6,653,988	8,990	—	—	—	—	—
Conversion of promissory notes and accrued interest to Series D redeemable convertible preferred stock	4,975,260	6,086	—	—	—	—	—
Issuance of common stock upon exercise of stock options	—	—	100,921	—	13	—	13
Stock-based compensation expense	—	—	—	—	121	—	121
Accretion of redeemable convertible preferred stock to redemption value	—	67	—	—	(67)	—	(67)
Net loss	—	—	—	—	—	(13,880)	(13,880)
<b>Balances at December 31, 2012</b>	73,991,017	62,785	4,622,336	5	146	(54,880)	(54,729)
Issuance of Series D redeemable convertible preferred stock, net of issuance costs of \$1	4,381,914	5,955	—	—	—	—	—
Issuance of Series E redeemable convertible preferred stock, net of issuance costs of \$156	16,110,473	34,844	—	—	—	—	—
Repurchase and retirement of common stock, at cost	—	—	(41,667)	—	—	—	—
Stock-based compensation expense	—	—	—	—	395	—	395
Accretion of redeemable convertible preferred stock to redemption value	—	213	—	—	(213)	—	(213)
Net loss	—	—	—	—	—	(14,027)	(14,027)
<b>Balances at December 31, 2013</b>	<u>94,483,404</u>	<u>\$103,797</u>	<u>4,580,669</u>	<u>\$ 5</u>	<u>\$ 328</u>	<u>\$ (68,907)</u>	<u>\$ (68,574)</u>

The accompanying notes are an integral part of these consolidated financial statements.

**ZAFGEN, INC.**  
**(A Development Stage Company)**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**  
**(In thousands)**

	Year Ended December 31,			Cumulative Period From Inception (November 22, 2005) to December 31, 2013
	2011	2012	2013	
<b>Cash flows from operating activities:</b>				
Net loss	\$(13,157)	\$(13,880)	\$(14,027)	\$ (68,828)
Adjustments to reconcile net loss to net cash used in operating activities				
Stock-based compensation expense	80	121	395	756
Non-cash interest expense	—	97	—	106
Depreciation expense	4	11	12	42
Unrealized foreign currency transaction losses	—	—	250	250
(Gain) loss on disposal of property and equipment	(2)	—	—	30
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(61)	(269)	165	(192)
Tax incentive receivable	—	(630)	(1,237)	(1,867)
Accounts payable	(43)	727	237	1,468
Accrued expenses	905	234	(799)	900
Net cash used in operating activities	<u>(12,274)</u>	<u>(13,589)</u>	<u>(15,004)</u>	<u>(67,335)</u>
<b>Cash flows from investing activities:</b>				
Purchases of property and equipment	(35)	(2)	(17)	(130)
Proceeds from sales of property and equipment	2	—	—	21
Deposits	(12)	—	—	(32)
Net cash used in investing activities	<u>(45)</u>	<u>(2)</u>	<u>(17)</u>	<u>(141)</u>
<b>Cash flows from financing activities:</b>				
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	10,069	16,057	40,799	96,473
Issuance of convertible promissory notes, net of issuance costs	—	5,989	—	6,664
Proceeds from issuance of common stock	—	—	—	38
Proceeds from exercise of common stock options	—	13	—	15
Repurchase of common stock at cost	—	—	—	(1)
Payments of initial public offering costs	—	—	(196)	(196)
Net cash provided by financing activities	<u>10,069</u>	<u>22,059</u>	<u>40,603</u>	<u>102,993</u>
<b>Net increase (decrease) in cash and cash equivalents</b>	<u>(2,250)</u>	<u>8,468</u>	<u>25,582</u>	<u>35,517</u>
Cash and cash equivalents at beginning of period	3,717	1,467	9,935	—
Cash and cash equivalents at end of period	<u>\$ 1,467</u>	<u>\$ 9,935</u>	<u>\$ 35,517</u>	<u>\$ 35,517</u>
<b>Supplemental disclosure of non-cash investing and financing activities:</b>				
Accretion of redeemable convertible preferred stock to redemption values	<u>\$ 53</u>	<u>\$ 67</u>	<u>\$ 213</u>	<u>\$ 554</u>
Conversion of convertible promissory notes and accrued interest to shares of redeemable convertible preferred stock	<u>\$ —</u>	<u>\$ 6,086</u>	<u>\$ —</u>	<u>\$ 6,770</u>
Deferred offering costs included in accounts payable	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 547</u>	<u>\$ 547</u>

The accompanying notes are an integral part of these consolidated financial statements.

**ZAFGEN, INC.**  
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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**  
**(Amounts in thousands, except share and per share data)**

**1. Nature of the Business and Basis of Presentation**

Zafgen, Inc. (the “Company”) (a development stage company) was incorporated on November 22, 2005 under the laws of the State of Delaware. The Company is a biopharmaceutical company dedicated to significantly improving the health and well-being of patients affected by obesity. Beloranib, the Company’s lead product candidate, is a novel, first-in-class, twice-weekly subcutaneous injection being developed for the treatment of multiple indications, including obesity and hyperphagia in Prader-Willi Syndrome patients, craniopharyngioma-associated obesity, and severe obesity in the general population. Since its inception, the Company has devoted substantially all of its efforts to research and development, recruiting management, acquiring operating assets and raising capital. Accordingly, the Company is considered to be in the development stage.

The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, new technological innovations, protection of proprietary technology, dependence on key personnel, compliance with government regulations and the need to obtain additional financing. Product candidates currently under development will require significant additional research and development efforts, including extensive pre-clinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure, and extensive compliance-reporting capabilities.

The Company’s product candidates are all in the development stage. There can be no assurance that the Company’s research and development will be successfully completed, that adequate protection for the Company’s intellectual property will be obtained, that any products developed will obtain necessary government regulatory approval or that any approved products will be commercially viable. Even if the Company’s product development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales. The Company operates in an environment of rapid change in technology and substantial competition from pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its employees and consultants.

The Company’s consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business. The Company has experienced negative cash flows and has a deficit accumulated during the development stage of \$68,907 as of December 31, 2013. The Company expects that its existing cash and cash equivalents as of December 31, 2013 will enable the Company to fund its operating expenses and capital expenditures requirements for at least twelve months. The future viability of the Company is largely dependent on its ability to generate cash from operating activities or to raise additional capital to finance its operations. The Company’s failure to raise capital as and when needed could have a negative impact on its financial condition and ability to pursue its business strategies.

The Company is seeking to complete an initial public offering of its common stock. Upon a successful qualified public offering with net proceeds of not less than \$35,000, the Company’s outstanding redeemable convertible preferred stock will automatically convert into shares of common stock.

In the event the Company does not complete an initial public offering, the Company expects to seek additional funding through private financings, debt financing, collaboration agreements or government grants. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into collaboration arrangements or obtain government grants. The terms of any financing may

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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**  
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adversely affect the holdings or the rights of the Company's stockholders. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects. Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries, Zafgen Securities Corporation, Zafgen Australia Pty Limited, and Zafgen Animal Health, LLC. All significant intercompany balances and transactions have been eliminated.

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP").

At December 31, 2013, the Company is considered a development stage enterprise. Until planned principal operations have commenced and significant revenue is generated, financial statements prepared in accordance with GAAP are required to report cumulative statements of operations and comprehensive loss, stockholders' equity (deficit) and cash flows from date of inception of the company.

## **2. Summary of Significant Accounting Policies**

### **Use of Estimates**

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual of research and development expenses and the valuation of common stock and stock-based awards. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Actual results could differ from the Company's estimates.

### **Unaudited Pro Forma Information**

The accompanying unaudited pro forma consolidated balance sheet as of December 31, 2013 has been prepared to give effect to the automatic conversion of all outstanding shares of redeemable convertible preferred stock into 99,064,073 shares of common stock as if the proposed initial public offering had occurred on December 31, 2013. In the accompanying consolidated statements of operations, unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2013 has been prepared to give effect to the automatic conversion of all outstanding shares of redeemable convertible preferred stock as if the proposed initial public offering had occurred on the later of January 1, 2013 or the issuance date of the redeemable convertible preferred stock.

### **Cash Equivalents**

The Company considers all short-term, highly liquid investments with original maturities of ninety days or less at acquisition date to be cash equivalents. Cash equivalents, which consist of money market accounts, are stated at fair value.



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**Concentration of Credit Risk and of Significant Suppliers**

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company has all cash and cash equivalents balances at one accredited financial institution, in amounts that exceed federally insured limits. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on third-party manufacturers to supply products for research and development activities in its programs. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

**Fair Value Measurements**

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices) such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's cash equivalents of \$8,001 and \$26,501 as of December 31, 2012 and 2013, respectively, were carried at fair value based on quoted prices in active markets, a Level 1 measurement. The carrying values of accounts payable and accrued expenses approximate their fair value due to the short-term nature of these liabilities.

**Deferred Offering Costs**

The Company capitalizes certain legal, accounting and other third-party fees that are directly associated with in-process equity financings as other assets until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' equity (deficit) as a reduction of additional paid-in capital generated as a result of the offering or as a reduction to the carrying value of preferred stock issued, if such stock is classified outside of stockholders' equity (deficit). As of December 31, 2013, the Company recorded \$743 in deferred offering costs in the accompanying consolidated balance sheet in contemplation of a probable 2014 equity financing. Should the equity financing no longer be considered probable of being consummated, the deferred offering costs would be expensed immediately as a charge to operating expenses in the consolidated statement of operations. The Company did not record any deferred offering costs as of December 31, 2012.

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**Property and Equipment**

Property and equipment are stated at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method over a five-year estimated useful life for both furniture and fixtures and office equipment. Expenditures for repairs and maintenance of assets are charged to expense as incurred. Upon retirement or sale, the cost and related accumulated depreciation of assets disposed of are removed from the accounts and any resulting gain or loss is included in loss from operations.

**Impairment of Long-Lived Assets**

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any impairment losses on long-lived assets.

**Research and Development Costs**

Research and development costs are expensed as incurred. Included in research and development expenses are wages, stock-based compensation and benefits of employees, third-party license fees and other operational costs related to the Company's research and development activities, including facility-related expenses and external costs of outside vendors engaged to conduct both pre-clinical studies and clinical trials. The Company records research and development expenses net of any research and development tax incentives the Company is entitled to receive from government authorities.

**Research Contract Costs and Accruals**

The Company has entered into various research and development contracts with research institutions and other companies both inside and outside of the United States. These agreements are generally cancelable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

**Patent Costs**

All patent-related costs incurred in connection with filing and prosecuting patent applications are recorded as general and administrative expenses as incurred, as recoverability of such expenditures is uncertain.

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**Accounting for Stock-Based Compensation**

The Company measures all stock options and other stock-based awards granted to employees and directors at the fair value on the date of the grant using the Black-Scholes option-pricing model. The fair value of the awards is recognized as expense, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. The straight-line method of expense recognition is applied to all awards with service-only conditions.

For stock-based awards granted to consultants and nonemployees, compensation expense is recognized over the period during which services are rendered by such consultants and nonemployees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is re-measured using the then-current fair value of the Company's common stock and updated assumption inputs in the Black-Scholes option-pricing model.

The Company classifies stock-based compensation expense in its consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipients' service payments are classified.

The Company recognizes compensation expense for only the portion of awards that are expected to vest. In developing a forfeiture rate estimate, the Company has considered its historical experience to estimate pre-vesting forfeitures for service-based awards. The impact of a forfeiture rate adjustment will be recognized in full in the period of adjustment, and if the actual forfeiture rate is materially different from the Company's estimate, the Company may be required to record adjustments to stock-based compensation expense in future periods.

**Income Taxes**

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred taxes are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect in the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

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**Segment Data**

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's singular focus is on advancing novel therapeutics for patients suffering from severe obesity and obesity-related disorders. No revenue has been generated since inception, and all tangible assets are held in the United States.

**Comprehensive Loss**

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. For the years ended December 31, 2011, 2012 and 2013 and for the cumulative period from inception (November 22, 2005) through December 31, 2013, there was no difference between net loss and comprehensive loss.

**Net Income (Loss) Per Share**

The Company follows the two-class method when computing net income (loss) per share, as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed.

Basic net income (loss) per share attributable to common stockholders is computed by dividing the net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) attributable to common stockholders is computed by adjusting income (loss) attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities, including outstanding stock options and unvested restricted common stock. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding for the period, including potential dilutive common shares assuming the dilutive effect of outstanding stock options and unvested restricted common stock.

The Company's redeemable convertible preferred stock contractually entitles the holders of such shares to participate in dividends but does not contractually require the holders of such shares to participate in losses of the Company. Similarly, restricted stock awards granted by the Company entitle the holder of such awards to dividends declared or paid by the board of directors, regardless of whether such awards are unvested, as if such shares were outstanding common shares at the time of the dividend. However, the unvested restricted stock awards are not entitled to share in the residual net assets (deficit) of the Company. Accordingly, in periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss attributable to common stockholders for the years ended December 31, 2011, 2012 and 2013.

**Recently Issued and Adopted Accounting Pronouncements**

In June 2011, the Financial Accounting Standards Board ("FASB") issued an amendment to the accounting guidance for presentation of comprehensive income. Under the amended guidance, a company may present the total of comprehensive income, the components of net income, and the components of other comprehensive income

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either in a single continuous statement of comprehensive income or in two separate but consecutive statements. In either case, a company is required to present each component of net income along with total net income, each component of other comprehensive income along with a total for other comprehensive income, and a total amount for comprehensive income. The amendment is effective for fiscal years ending, and interim periods within those years, beginning after December 15, 2011, and is applied retrospectively. The Company adopted this amendment in the accompanying consolidated financial statements by presenting comprehensive loss in a single continuous statement along with net loss.

Accounting standards that have been issued or proposed by the FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on the Company's consolidated financial statements upon adoption.

**3. Property and Equipment, net**

Property and equipment, net consisted of the following as of December 31, 2012 and 2013:

	<b>December 31,</b>	
	<b>2012</b>	<b>2013</b>
Office equipment	\$ 10	\$ 27
Furniture and fixtures	44	44
	54	71
Less: Accumulated depreciation	(22)	(34)
	<u>\$ 32</u>	<u>\$ 37</u>

Depreciation expense was \$4, \$11 and \$12 for the years ended December 31, 2011, 2012 and 2013, respectively, and \$42 for the period from inception (November 22, 2005) through December 31, 2013.

**4. Accrued Expenses**

Accrued expenses consisted of the following as of December 31, 2012 and 2013:

	<b>December 31,</b>	
	<b>2012</b>	<b>2013</b>
Accrued payroll and related expenses	\$ 74	\$ 49
Accrued research and development expenses	1,558	616
Accrued professional fees	62	196
Accrued other	5	39
	<u>\$1,699</u>	<u>\$900</u>

**5. Convertible Promissory Notes**

In 2006, the Company issued promissory notes with a principal amount of \$175. In August 2006, the Company and noteholders agreed to convert the outstanding principal into shares of the Company's newly issued Series A redeemable convertible preferred stock at a price of \$0.294 per share for a total of 595,238 shares (see Note 6).

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In July 2007, the Company issued a convertible promissory note with a principal amount of \$500. The note accrued interest at an annual rate of 8%. If not converted prior to maturity, principal and interest were payable at the stated maturity date of December 31, 2007 or, at the election of the noteholder, could be converted into Series A redeemable convertible preferred stock at a per share price of \$0.388. Effective upon the closing of a financing of at least \$3,000 (a "Qualified Financing"), all of the outstanding principal and interest under the note automatically converted into shares of the same class and series of capital stock as issued to others in the Qualified Financing at a conversion price of 80% of the price per share of the capital stock issued in the Qualified Financing. The Qualified Financing occurred in October 2007, at which time principal and accrued interest of \$509 was converted into 842,497 shares of Series B redeemable preferred stock at an issuance price of \$0.60 per share.

In August and November 2012, the Company issued convertible promissory notes with a principal amount of \$6,000. The notes accrued interest at an annual rate of 8% and, unless otherwise converted, were due one year from the issuance date. The notes were to be automatically converted into shares of a new class of preferred stock upon the sale by the Company of the new class of preferred stock yielding proceeds of at least \$10,000 or, if the sale of the new class of preferred stock was for less than \$10,000, the notes could be converted at the option of the noteholder at 90% of the price of the new series of preferred stock. In November 2012, upon the Company's issuance of 6,653,988 shares of Series D redeemable convertible preferred stock for gross proceeds of \$9,044 (see Note 6), the noteholders elected to convert the outstanding principal and accrued interest of \$6,086 into 4,975,260 shares of Series D redeemable convertible preferred stock.

#### **6. Redeemable Convertible Preferred Stock**

As of December 31, 2013, the Company's Certificate of Incorporation, as amended and restated, authorizes the Company to issue 99,292,610 shares of \$0.001 par value preferred stock.

The Company has issued Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock (collectively, the "Redeemable Preferred Stock"). The Redeemable Preferred Stock is classified outside of stockholders' equity (deficit) because the shares contain redemption features that are not solely within the control of the Company.

During 2006 and 2007, the Company issued a total of 4,768,001 shares of Series A redeemable convertible preferred stock at an issuance price equal to \$0.419463 per share and received gross proceeds of \$2,000. In connection with these financings, the Company paid total issuance costs of \$82. Additionally, in 2006, \$175 of convertible promissory notes were converted into 595,238 shares of Series A redeemable convertible preferred stock (see Note 5).

During 2007, 2008 and 2010, the Company issued a total of 36,741,738 shares of Series B redeemable convertible preferred stock at an issuance price equal to \$0.75503 per share and received gross proceeds of \$27,741. In connection with these financings, the Company paid total issuance costs of \$111. Additionally, in 2007, a convertible promissory note of \$500 and accrued interest of \$9 were converted into 842,497 shares of Series B redeemable convertible preferred stock (see Note 5). In February 2011, the Company issued a total of 2,682,011 shares of Series B redeemable convertible preferred stock at an issuance price equal to \$0.75503 per share and received gross proceeds of \$2,025. In connection with this financing, the Company paid total issuance costs of \$9.

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In June and December 2011, the Company issued a total of 8,923,884 shares of Series C redeemable convertible preferred stock at an issuance price equal to \$0.9061 per share and received gross proceeds of \$8,086. In connection with this financing, the Company paid total issuance costs of \$33.

In February 2012, the Company issued 7,808,400 shares of Series C redeemable convertible preferred stock at an issuance price equal to \$0.9061 per share and received gross proceeds of \$7,075. In connection with this financing, the Company paid total issuance costs of \$8.

In November 2012, the Company issued 6,653,988 shares of Series D redeemable convertible preferred stock at an issuance price equal to \$1.3592 per share and received gross proceeds of \$9,044. In connection with this financing, the Company paid total issuance costs of \$54. Additionally, in November 2012, \$6,000 of convertible promissory notes and \$86 of accrued interest were converted into 4,975,260 shares of Series D redeemable convertible preferred stock (see Note 5).

In January 2013, the Company issued 4,381,914 shares of Series D redeemable convertible preferred stock at an issuance price equal to \$1.3592 per share and received gross proceeds of \$5,956. In connection with this financing, the Company paid total issuance costs of \$1.

In November 2013, the Company issued 16,110,473 shares of Series E redeemable convertible preferred stock at an issuance price equal to \$2.1725 per share and received gross proceeds of \$35,000. In connection with this financing, the Company paid total issuance costs of \$156.

Redeemable Preferred Stock consisted of the following as of December 31, 2012:

	Preferred Shares Authorized	Preferred Shares Issued and Outstanding	Liquidation Preference	Carrying Value	Common Stock Issuable Upon Conversion
Series A redeemable convertible preferred stock	5,363,239	5,363,239	\$ 2,250	\$ 2,222	5,363,239
Series B redeemable convertible preferred stock	40,266,246	40,266,246	30,402	30,335	40,266,246
Series C redeemable convertible preferred stock	16,732,284	16,732,284	15,161	15,137	16,732,284
Series D redeemable convertible preferred stock	16,011,162	11,629,248	15,816	15,091	11,629,248
	<u>78,372,931</u>	<u>73,991,017</u>	<u>\$ 63,629</u>	<u>\$62,785</u>	<u>73,991,017</u>

Redeemable Preferred Stock consisted of the following as of December 31, 2013:

	Preferred Shares Authorized	Preferred Shares Issued and Outstanding	Liquidation Preference	Carrying Value	Common Stock Issuable Upon Conversion
Series A redeemable convertible preferred stock	5,363,239	5,363,239	\$ 2,250	\$ 2,229	5,363,239
Series B redeemable convertible preferred stock	40,266,246	40,266,246	30,402	30,351	40,266,246
Series C redeemable convertible preferred stock	16,732,284	16,732,284	15,161	15,144	16,732,284
Series D redeemable convertible preferred stock	16,011,162	16,011,162	21,775	21,226	16,011,162
Series E redeemable convertible preferred stock	20,919,679	16,110,473	35,000	34,847	16,110,473
	<u>99,292,610</u>	<u>94,483,404</u>	<u>\$ 104,588</u>	<u>\$ 103,797</u>	<u>94,483,404</u>

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The holders of the Redeemable Preferred Stock have the following rights and preferences:

**Voting Rights**

The holders of Redeemable Preferred Stock are entitled to vote, together with the holders of common stock, on all matters submitted to stockholders for a vote. Holders of all Redeemable Preferred Stock have the right to vote the number of shares equal to the number of shares of common stock into which such Redeemable Preferred Stock could convert on the record date for determination of stockholders entitled to vote.

**Dividends**

The Company may not declare, pay or set aside any dividends on shares of any other class or series of capital stock of the Company unless the holders of the Redeemable Preferred Stock then outstanding shall first receive a dividend on each outstanding share of Redeemable Preferred Stock in an amount at least equal to (i) in the case of a dividend on common stock or any class or series that is convertible into common stock, that dividend per share of Redeemable Preferred Stock as would equal the product of (A) the dividend payable on each share of such class or series determined, if applicable, as if all shares of such class or series had been converted into common stock and (B) the number of shares of common stock issuable upon conversion of a share of Redeemable Preferred Stock determined by (A) dividing the amount of the dividend payable on each share of such class or series of capital stock by the original issuance price of such class or series of capital stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination of or other similar recapitalization affecting such shares) and (B) multiplying such fraction by an amount equal to the Original Issue Price (as defined below) of each series of Redeemable Preferred Stock. If the Company declares, pays or sets aside, on the same date, a dividend on shares of more than one class or series of capital stock of the Company, the dividend payable to the holders of the Redeemable Preferred Stock shall be calculated based upon the dividend on the class or series of capital stock that would result in the highest Redeemable Preferred Stock dividend. The Original Issue Price for Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock is \$0.419463, \$0.75503, \$0.9061, \$1.3592 and \$2.1725, respectively, per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Redeemable Preferred Stock.

**Liquidation Preference**

In the event of any liquidation, voluntary or involuntary, exclusive out-license of all or substantially all of the intellectual property of the Company, dissolution or winding up of the Company or Deemed Liquidation Event (as defined below), the Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stockholders are entitled to receive, in preference to all other stockholders, and to the extent available, an amount equal to the Original Issue Price per share, adjusted for any stock dividends, stock splits or reclassifications, plus all dividends declared but unpaid. In the event that proceeds are not sufficient to permit payment in full to these holders, the proceeds will be ratably distributed among the Series A, Series B, Series C, Series D and Series E holders in proportion to the full preferential amount each such holder is otherwise entitled to receive.

After payments have been made in full to the holders of the Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock, then, to the extent available, holders of the common stock and holders of the Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock will



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receive the remaining amounts available for distribution ratably in proportion to the number of common shares held by them or issuable to them upon conversion of their redeemable convertible preferred stock into common stock. The distributions are subject to an overall distribution limit of the greater of (i) two times the amount the holders of the Redeemable Preferred Stock are entitled to based on their preference payment and (ii) the amount such holder would have received if such holder had converted shares of the Redeemable Preferred Stock into common stock immediately prior to such dissolution, liquidation, exclusive out-license of all or substantially all of the intellectual property, or winding up of the Company or Deemed Liquidation Event.

Unless the holders of at least 70% of the then outstanding shares of the Redeemable Preferred Stock, voting together as a single class on an as-converted basis, elect otherwise, a Deemed Liquidation Event shall include a sale of the Company, a sale of the capital stock representing a majority of the voting power or a merger or consolidation of the Company into or with another corporation in which the existing Company holds less than a majority of the voting power of the surviving or resulting corporation, or the sale, lease, transfer, exclusive license or other disposition, in a single transaction or series of related transactions, by the Company of all or substantially all of the assets of the Company.

**Conversion**

Each share of Redeemable Preferred Stock is convertible into common stock at the option of the stockholder at any time after the date of issuance. Each share of the preferred stock will automatically be converted into shares of common stock, at the applicable Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock conversion ratio then in effect, upon a qualified public offering with net proceeds of not less than \$35,000. The conversion ratio of the Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock, as defined, is determined by dividing the Original Issue Price of each series of preferred stock by the Conversion Price of each series. The Conversion Price of each series shall initially be \$0.419463 for Series A, \$0.75503 for Series B, \$0.90610 for Series C, \$1.3592 for Series D and \$2.1725 for Series E. The Conversion Price is subject to adjustment as set forth in the Company's Certificate of Incorporation, as amended and restated, unless at least a majority of the Series A holders, at least 70% of each of Series B or Series C holders, at least 65% of Series D holders and at least a majority of the Series E holders, voting separately as a class with respect to their series, agree that no such adjustment shall be made to their series. As of December 31, 2013, all outstanding shares of Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock were convertible into common stock on a 1-for-1 basis.

**Redemption Rights**

At the written election of at least 70% of the holders of the Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock, voting together as a single class on an as-converted basis, the shares of Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock outstanding are redeemable, at any time on or after November 22, 2017, in three equal annual installments commencing sixty days after receipt of the required vote at the Original Issue Price per share of Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock plus all declared but unpaid dividends thereon.

The carrying values of the Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock are being accreted to their redemption values through their respective redemption dates.

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**Reissuance**

Shares of any Series A, Series B, Series C, Series D or Series E redeemable convertible preferred stock that are redeemed or converted will be retired or canceled and not reissued by the Company.

**7. Common Stock**

As of December 31, 2013, the Company's Certificate of Incorporation, as amended and restated, authorizes the Company to issue 115,000,000 shares of \$0.001 par value common stock.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the board of directors, if any, subject to the preferential dividend rights of the Redeemable Preferred Stock. When dividends are declared on shares of common stock, the Company must declare at the same time a dividend payable to the holders of Redeemable Preferred Stock equivalent to the dividend amount they would receive if each preferred share were converted into common stock. The Company may not pay dividends to common stockholders until all dividends accrued or declared but unpaid on the Redeemable Preferred Stock have been paid in full. As of December 31, 2013, no dividends had been declared.

During the year ended December 31, 2013, the Company reacquired and retired 41,667 shares of restricted common stock, at cost, that were forfeited by a former employee.

As of December 31, 2013, the Company had reserved 105,043,636 shares of common stock for the conversion of the outstanding shares of Series A, Series B, Series C, Series D and Series E redeemable convertible preferred stock (see Note 6) and the exercise of stock options and issuance of common stock under the Company's Amended and Restated 2006 Stock Option Plan (see Note 8).

**8. Stock-Based Awards**

**2006 Stock Option Plan**

The Company's Amended and Restated 2006 Stock Option Plan (the "2006 Plan") provides for the Company to sell or issue common stock or restricted common stock, or to grant incentive stock options or nonqualified stock options for the purchase of common stock, to employees, members of the board of directors and consultants of the Company. The 2006 Plan is administered by the board of directors, or at the discretion of the board of directors, by a committee of the board. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, or their committee if so delegated, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the share of common stock on the date of grant and the term of stock option may not be greater than ten years.

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Stock options granted under the 2006 Plan generally vest over four years and expire after ten years, although options have been granted with vesting terms less than four years.

The total number of shares of common stock that may be issued under the 2006 Plan was 11,863,864 shares as of December 31, 2013, of which 2,331,257 shares remained available for future grant at December 31, 2013.

The Company generally grants stock-based awards with service conditions only (“service-based” awards).

As required by the 2006 Plan, the exercise price for stock options granted is not to be less than the fair value of common shares as determined by the Company as of the date of grant. The Company values its common stock by taking into consideration its most recently available valuation of common shares performed by management and the board of directors as well as additional factors which may have changed since the date of the most recent contemporaneous valuation through the date of grant.

**Stock Option Valuation**

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. The Company historically has been a private company and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company’s stock options has been determined utilizing the “simplified” method for awards that qualify as “plain-vanilla” options. The expected term of stock options granted to nonemployees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future. The assumptions that the Company used to determine the fair value of the stock options granted to employees and directors are as follows, presented on a weighted average basis (the Company did not grant any stock options to employees or directors during the year ended December 31, 2012):

	<u>Year Ended December 31,</u>	
	<u>2011</u>	<u>2013</u>
Risk-free interest rate	1.41%	1.12%
Expected term (in years)	6.25	6.25
Expected volatility	78%	85%
Expected dividend yield	0%	0%

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The following table summarizes the Company's stock option activity since January 1, 2011:

	<u>Shares Issuable Under Options</u>	<u>Weighted Average Exercise Price</u>	<u>Weighted Average Remaining Contractual Term (In years)</u>	<u>Aggregate Intrinsic Value</u>
<b>Outstanding as of January 1, 2011</b>	2,765,148	\$ 0.12	8.5	\$ 216
Granted	2,988,000	0.25		
Exercised	—	—		
Forfeited	—	—		
<b>Outstanding as of December 31, 2011</b>	<u>5,753,148</u>	\$ 0.19	8.7	\$ 354
Granted	50,000	0.25		
Exercised	(100,921)	0.14		
Forfeited	(1,988,000)	0.25		
<b>Outstanding as of December 31, 2012</b>	<u>3,714,227</u>	\$ 0.16	7.1	\$ 342
Granted	4,514,748	0.42		
Exercised	—	—		
Forfeited	—	—		
<b>Outstanding as of December 31, 2013</b>	<u>8,228,975</u>	\$ 0.30	7.8	\$ 10,185
<b>Options vested and expected to vest as of December 31, 2013</b>	<u>8,228,975</u>	\$ 0.30	7.8	\$ 10,185
<b>Options exercisable as of December 31, 2013</b>	<u>4,128,016</u>	\$ 0.20	6.6	\$ 5,543

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock. The aggregate intrinsic value of stock options exercised was \$12 during the year ended December 31, 2012. No stock options were exercised during the years ended December 31, 2011 or 2013.

The Company received cash proceeds from the exercise of stock options of \$13 during the year ended December 31, 2012.

The weighted average grant-date fair value of stock options granted to employees and directors during the years ended December 31, 2011 and 2013 was \$0.17 and \$0.29 per share, respectively. The Company did not grant stock options to employees or directors in 2012. The grant of stock options in 2012 was to a consultant.

As of December 31, 2013, there were outstanding unvested service-based stock options held by nonemployees for the purchase of 110,000 shares of common stock. Additionally as of December 31, 2013, there were outstanding unvested performance-based stock options held by nonemployees for the purchase of 5,000 shares of common stock.

**Restricted Common Stock**

The 2006 Plan provides for the award of restricted stock. The Company has granted restricted common stock with time-based vesting conditions. Unvested shares of restricted common stock may not be sold or transferred by the holder. These restrictions lapse according to the time-based vesting conditions of each award.

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The table below summarizes the Company's restricted stock activity since January 1, 2011:

	Shares	Weighted Average Grant- Date Fair Value
<b>Unvested restricted common stock as of January 1, 2011</b>	241,667	\$ 0.13
Issued	—	—
Vested	(87,500)	0.12
Forfeited	—	—
<b>Unvested restricted common stock as of December 31, 2011</b>	154,167	\$ 0.13
Issued	—	—
Vested	(87,500)	0.12
Forfeited	—	—
<b>Unvested restricted common stock as of December 31, 2012</b>	66,667	\$ 0.13
Issued	—	—
Vested	(25,000)	0.12
Forfeited	(41,667)	0.13
<b>Unvested restricted common stock as of December 31, 2013</b>	—	—

The aggregate intrinsic value of restricted stock awards is calculated as the difference between the grant-date fair value of the restricted stock awards and the fair value of the Company's common stock. The aggregate intrinsic value of restricted stock awards that vested during each of the years ended December 31, 2011, 2012 and 2013 was \$22, \$22 and \$38, respectively. As of December 31, 2013, there were no unvested restricted stock awards subject to repurchase.

**Stock-based Compensation**

The Company recorded stock-based compensation expense related to stock options and restricted common stock in the following expense categories of its statements of operations:

	Year Ended December 31,			Cumulative Period From Inception (November 22, 2005) to December 31, 2013
	2011	2012	2013	
Research and development	\$ 30	\$ 68	\$ 176	\$ 339
General and administrative	50	53	219	417
	<u>\$ 80</u>	<u>\$ 121</u>	<u>\$ 395</u>	<u>\$ 756</u>

As of December 31, 2013, the Company had an aggregate of \$1,334 of unrecognized stock-based compensation cost, which is expected to be recognized over a weighted average period of 3.6 years.

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**9. Net Loss Per Share and Unaudited Pro Forma Net Loss Per Share****Net Loss Per Share**

Basic and diluted net loss per share attributable to common stockholders was calculated as follows for the years ended December 31, 2011, 2012 and 2013:

	<u>Year Ended December 31,</u>		
	<u>2011</u>	<u>2012</u>	<u>2013</u>
<b>Numerator:</b>			
Net loss	\$ (13,157)	\$ (13,880)	\$ (14,027)
Accretion of redeemable convertible preferred stock to redemption value	(53)	(67)	(213)
Net loss attributable to common stockholders	<u>\$ (13,210)</u>	<u>\$ (13,947)</u>	<u>\$ (14,240)</u>
<b>Denominator:</b>			
Weighted average common shares outstanding, basic and diluted	<u>4,326,581</u>	<u>4,456,778</u>	<u>4,578,127</u>
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (3.05)</u>	<u>\$ (3.13)</u>	<u>\$ (3.11)</u>

The Company excluded the following common stock equivalents, outstanding as of December 31, 2011, 2012 and 2013, from the computation of diluted net loss per share attributable to common stockholders for the years ended December 31, 2011, 2012 and 2013 because they had an anti-dilutive impact due to the net loss attributable to common stockholders incurred for the periods.

	<u>December 31,</u>		
	<u>2011</u>	<u>2012</u>	<u>2013</u>
Stock options to purchase common stock	5,753,148	3,714,227	8,228,975
Unvested restricted common stock	154,167	66,667	—
	<u>5,907,315</u>	<u>3,780,894</u>	<u>8,228,975</u>

**Unaudited Pro Forma Net Loss Per Share**

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2013 gives effect to adjustments arising upon the closing of a qualified initial public offering. The unaudited pro forma net loss attributable to common stockholders used in the calculation of unaudited basic and diluted pro forma net loss per share attributable to common stockholders does not include the effects of the accretion on redeemable convertible preferred stock, because it assumes that the conversion of redeemable convertible preferred stock into common stock had occurred on the later of January 1, 2013 or the issuance date of the redeemable convertible preferred stock.

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The unaudited pro forma basic and diluted weighted average common shares outstanding used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2013 gives effect to the automatic conversion upon a qualified initial public offering of all outstanding shares of redeemable convertible preferred stock as of December 31, 2013 into 94,483,404 shares of common stock as if the conversion had occurred on the later of January 1, 2013 or the issuance date of the redeemable convertible preferred stock.

The computation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders is as follows:

	<b>Year Ended December 31, 2013 (unaudited)</b>
<b>Numerator:</b>	
Net loss	\$ (14,027)
Pro forma net loss attributable to common stockholders	<u>\$ (14,027)</u>
<b>Denominator:</b>	
Weighted average common shares outstanding, basic and diluted	4,578,127
Pro forma adjustment for assumed automatic conversion of all outstanding shares of redeemable convertible preferred stock upon the closing of the proposed initial public offering	<u>79,611,438</u>
Pro forma weighted average common shares outstanding, basic and diluted	<u>84,189,565</u>
Pro forma net loss per share attributable to common stockholders, basic and diluted	<u>\$ (0.17)</u>

**10. Commitments and Contingencies**

**Leases**

The Company leases its office space under an operating lease agreement that initially expired on July 31, 2013, but was amended in 2013 to extend the lease through January 31, 2014. The lease, as amended, allows for up to two six-month extension periods. In December 2013, the Company extended the lease through July 31, 2014, cancellable with 30 days' notice.

Future minimum lease payments for its operating lease as of December 31, 2013 were as follows:

<b>Year ending December 31,</b>	
2014	<u>\$64</u>
Total	<u>\$64</u>

The Company also leased laboratory space in prior years; however, these leases terminated prior to 2011 and, as of December 31, 2013, there are no future commitments for laboratory space. During the years ended December 31, 2011, 2012 and 2013, the Company recognized \$102, \$129 and \$105, respectively, of rental expense related to office space. For the period from inception (November 22, 2005) through December 31, 2013, the Company recognized \$882 of rental expense related to office and laboratory space.

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**Intellectual Property Licenses**

The Company has acquired exclusive rights to develop patented compounds and related know-how for beloranib under two licensing agreements with two third parties in the course of its research and development activities. The licensing rights obligate the Company to make payments to the licensors for license fees, milestones, license maintenance fees and royalties. The Company is also responsible for patent prosecution costs. Related to these license agreements, the Company made payments and recorded research and development expenses in its consolidated statements of operations as follows:

	<u>Year Ended December 31,</u>			<u>Cumulative Period</u>
	<u>2011</u>	<u>2012</u>	<u>2013</u>	<u>From Inception</u>
				<u>(November 22, 2005)</u>
				<u>to December 31,</u>
				<u>2013</u>
Licensing, milestone and license maintenance fees	<u>\$ 1,055</u>	<u>\$ 150</u>	<u>\$ —</u>	<u>\$ 2,365</u>

The Company is obligated to make additional milestone payments of up to \$18,950 upon reaching certain pre-commercialization milestones, such as clinical trials and government approvals, and up to \$12,500 upon reaching certain product commercialization milestones. Under one of the license agreements, the Company is also obligated to pay up to \$1,250 with respect to each subsequent licensed product, if any, that is a new chemical entity. In addition, the Company will owe single-digit royalties on sales of commercial products developed using these licensed technologies, if any. The Company is also obligated to pay to the licensors a percentage of fees received if and when the Company sublicenses the technology. As of December 31, 2013, the Company has not yet developed a commercial product using the licensed technologies and it has not entered into any sublicense agreements for the technologies.

**Indemnification Agreements**

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners, and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2012 or 2013.

**11. Income Taxes**

During the years ended December 31, 2011, 2012 and 2013, the Company recorded no income tax benefits for the net operating losses incurred in each year or interim period, due to its uncertainty of realizing a benefit from those items.



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**(A Development Stage Company)**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**  
**(Amounts in thousands, except share and per share data)**

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2011	2012	2013
Federal statutory income tax rate	(34.0%)	(34.0%)	(34.0%)
Federal and state research and development tax credit	(6.4)	(1.2)	(9.0)
Orphan drug tax credit	—	—	(3.1)
State taxes, net of federal benefit	(5.4)	(5.0)	(4.0)
Meals and entertainment	0.1	—	—
Stock-based compensation expense	0.2	0.2	0.6
Nondeductible Australia research and development expenses	—	1.8	4.1
Change in deferred tax asset valuation allowance	45.5	38.2	45.4
Effective income tax rate	<u>0.0%</u>	<u>0.0%</u>	<u>0.0%</u>

Net deferred tax assets as of December 31, 2012 and 2013 consisted of the following:

	December 31,	
	2012	2013
<b>Current deferred tax assets:</b>		
Accrued expenses	\$ 46	\$ 18
Other temporary differences	1	2
Total current deferred tax assets	<u>47</u>	<u>20</u>
<b>Noncurrent deferred tax assets:</b>		
Capitalized research and development expenses	16,676	19,856
Net operating loss carryforwards	3,209	4,021
Tax credit carryforwards	3,656	5,579
Capitalized legal expenses	385	790
Stock-based compensation	33	91
Total noncurrent deferred tax assets	<u>23,959</u>	<u>30,337</u>
Total gross deferred tax assets	24,006	30,357
Valuation allowance	<u>(24,006)</u>	<u>(30,357)</u>
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

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Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2011, 2012 and 2013 related primarily to the increase in net operating loss carryforwards, capitalized research and development expenses and research and development tax credit carryforwards and were as follows:

	Year Ended December 31,		
	2011	2012	2013
Valuation allowance as of beginning of year	\$ 12,748	\$ 18,744	\$ 24,006
Decreases recorded as benefit to income tax provision	—	—	—
Increases recorded to income tax provision	5,996	5,262	6,351
Valuation allowance as of end of year	<u>\$ 18,744</u>	<u>\$ 24,006</u>	<u>\$ 30,357</u>

As of December 31, 2013, the Company had net operating loss carryforwards for federal and state income tax purposes of \$10,548 and \$8,226, respectively, which begin to expire in 2026 and 2014, respectively. The Company also had an additional \$16 of federal and state net operating losses not reflected above that were attributable to stock option exercises, which will be recorded as an increase in additional paid-in capital once they are realized in accordance with accounting for stock-based compensation awards. As of December 31, 2013, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of \$4,706 and \$1,322, respectively, which begin to expire in 2026 and 2021, respectively. Utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed and any limitation is known, no amounts are being presented as an uncertain tax position.

As of December 31, 2012 and 2013, the Company's gross deferred tax asset balance of \$24,006 and \$30,357, respectively, was comprised principally of net operating loss carryforwards, capitalized research and development expenses and research and development tax credit carryforwards. During the years ended December 31, 2011, 2012 and 2013, gross deferred tax assets increased due to additional net operating loss carryforwards, research and development tax credits generated and additional research and development expenses capitalized for tax purposes.

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The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's history of cumulative net losses incurred since inception and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets as of December 31, 2012 and 2013. Management reevaluates the positive and negative evidence at each reporting period.

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2012 or 2013.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending income tax examinations. The Company's tax years are still open under statute from 2010 to the present. Earlier years may be examined to the extent that tax credit or net operating loss carryforwards are used in future periods. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision.

**12. Retirement Plan**

In 2009, the Company established a Savings Incentive Match Plan for employees. Under the terms of the plan, the Company contributes 2% of an employee's annual base salary, up to a maximum of the annual Internal Revenue Service compensation limits, for all full-time employees.

During the years ended December 31, 2011, 2012 and 2013, the Company recognized \$15, \$16 and \$26, respectively, of expense related to its contributions to this plan. During the period from inception (November 22, 2005) through December 31, 2013, the Company recognized \$78 of expense related to its contributions to this plan.

**13. Qualifying Therapeutic Discovery Project Program**

In 2010, the Company received \$489 for two research projects under the Qualifying Therapeutic Discovery Project Credit program under the Patient Protection and Affordable Care Act, covering 50% of qualifying expenses incurred. The Company recorded the proceeds as a reduction of research and development expenses in the consolidated statements of operations for the period from inception (November 22, 2005) through December 31, 2013.

**14. Australia Research and Development Tax Incentive**

The Australian government has established a research and development tax incentive to encourage industry investment in research and development, which is available to companies incorporated under an Australian law that have core research and development activities. The Company established Zafgen Australia Pty Limited, a wholly owned subsidiary, in October 2012 to carry out certain research and development activities. As this subsidiary meets the eligibility requirements of the Australian tax law, it is eligible to receive a 45% refundable tax incentive for qualified research and development activities. For the years ended December 31, 2012 and 2013, \$630 and \$1,237, respectively, have been recorded as a reduction to research and development expenses in the consolidated

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statements of operations, representing 45% of the Company's qualified research and development spending in Australia. For the period from inception (November 22, 2005) through December 31, 2013, \$1,867 has been recorded as a reduction to research and development expenses in the consolidated statements of operations. The refund is denominated in Australian dollars and, therefore, the receivable is re-measured into U.S. dollars as of each reporting date. For the year ended December 31, 2013, the Company recorded in its consolidated statements of operations unrealized foreign currency exchange losses of \$250 related to this tax incentive receivable. The Company did not have any foreign exchange gains or losses related to this receivable for periods prior to 2013. As of December 31, 2012 and 2013, the Company's tax incentive receivable from the Australian government was \$630 and \$1,617, respectively.

**15. Related Party Transactions**

In October 2011, the Company entered into an agreement with a member of the board of directors under which the board member would also serve as a business development consultant. Under the terms of the agreement, the annual consulting fee was \$80. Additionally, a success fee of \$500 would be earned upon a change in control of the Company. During the years ended December 31, 2011 and 2012, the Company paid the board member \$18 and \$80, respectively, for consulting services. This agreement was terminated in 2012.

**16. Subsequent Events**

For its consolidated financial statements as of December 31, 2013 and for the year then ended, the Company evaluated subsequent events through March 14, 2014, the date on which those consolidated financial statements were originally issued, and through April 28, 2014, the date on which those consolidated financial statements were reissued.

In February 2014, the Company issued 204,101 shares of Series E redeemable convertible preferred stock at a price of \$2.1725 per share for net proceeds of \$443.

**17. Subsequent Events (unaudited)**

**Credit Facility**

On March 31, 2014, the Company entered into a loan and security agreement (the "Credit Facility"). The Credit Facility provides for initial borrowings of \$7,500 under a term loan ("Term Loan A") and additional borrowings of up to \$12,500 under other term loans, for a maximum of \$20,000. On March 31, 2014, the Company received proceeds of \$7,500 from the issuance of promissory notes under the Term Loan A. Of the additional \$12,500 amount available, \$7,500 ("Term Loan B") is available to be drawn down until September 30, 2014 and \$5,000 ("Term Loan C") is available subject to the completion of an initial public offering with net cash proceeds to the Company of at least \$50,000 (a "Qualified IPO"). Upon a Qualified IPO, Term Loan C will be available to be drawn down through the earlier of December 31, 2014 or 30 days after the Qualified IPO. All promissory notes issued under the Credit Facility are due on December 1, 2017 and are collateralized by substantially all of the Company's personal property, other than its intellectual property. There are no financial covenants associated with the debt facility; however, there are negative covenants restricting the Company's activities, including limitations on dispositions, mergers or acquisitions; encumbering or granting a security interest in its intellectual property; incurring indebtedness or liens; paying dividends; making certain investments; and certain other business transactions.

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The Company is obligated to make monthly, interest-only payments on any term loans funded under the Credit Facility until December 1, 2014 and, thereafter, to pay 36 consecutive, equal monthly installments of principal and interest from January 1, 2015 through December 1, 2017. Upon a Qualified IPO, the term of monthly, interest-only payments will be extended until June 1, 2015. Term loans under the Credit Facility bear interest at an annual rate of 8.1%. In addition, a final payment equal to 6.0% of any amounts drawn under the Credit Facility is due upon the earlier of the maturity date, acceleration of the term loans or prepayment of all or part of the term loans.

The Company is obligated to pay a separate fee of up to \$450 upon any initial public offering; a sale of substantially all of the Company's assets; or a merger, reorganization or sale of the Company's voting equity securities where existing voting stockholders hold less than 50% of voting equity securities after such transaction.



**Shares**

**COMMON STOCK**

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**Preliminary Prospectus**

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*Joint Bookrunners*

**Leerink Partners**

**Cowen and Company**

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*Co-Managers*

**Canaccord Genuity**

**JMP Securities**

, 2014

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**PART II**  
**INFORMATION NOT REQUIRED IN PROSPECTUS**

**Item 13. Other Expenses of Issuance and Distribution**

The following table sets forth all expenses, other than the underwriting discounts and commissions, payable by Zafgen, Inc. (the “Company” or the “Registrant”) in connection with the sale of the common stock being registered. All the amounts shown are estimates except the SEC registration fee and the FINRA filing fee.

	<u>Amount</u>
SEC registration fee	\$11,109
FINRA filing fee	12,788
NASDAQ initial listing fee	*
Blue sky qualification fees and expenses	*
Printing and engraving expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer agent and registrar fees	*
Miscellaneous	*
Total	<u>\$</u> *

\* To be filed by amendment.

**Item 14. Indemnification of Directors and Officers**

Section 145 of the Delaware General Corporation Law permits a corporation to include in its charter documents, and in agreements between the corporation and its directors and officers, provisions expanding the scope of indemnification beyond that specifically provided by the current law.

Section 145(a) of the Delaware General Corporation Law provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation), because he or she is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys’ fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding, if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful.

Section 145(b) of the Delaware General Corporation Law provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor because the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys’ fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification shall be made with respect to any claim, issue or matter as to which he or she shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of

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the case, he or she is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or other adjudicating court shall deem proper.

Section 145(g) of the Delaware General Corporation Law provides, in general, that a corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of his or her status as such, whether or not the corporation would have the power to indemnify the person against such liability under Section 145 of the Delaware General Corporation Law.

The Company's amended and restated certificate of incorporation, which will become effective upon completion of the offering, provides for the indemnification of directors to the fullest extent permissible under Delaware law.

The Company's amended and restated by-laws, which will become effective upon completion of the offering, provide for the indemnification of officers, directors and third parties acting on the Company's behalf if such persons act in good faith and in a manner reasonably believed to be in and not opposed to the Company's best interest, and, with respect to any criminal action or proceeding, such indemnified party had no reason to believe his or her conduct was unlawful.

The Company is entering into indemnification agreements with each of its directors and executive officers, in addition to the indemnification provisions provided for in its charter documents, and the Company intends to enter into indemnification agreements with any new directors and executive officers in the future. These agreements will provide that we will indemnify each of our directors and executive officers, and such entities to the fullest extent permitted by law.

The underwriting agreement (to be filed as Exhibit 1.1 hereto) will provide for indemnification by the underwriters of the Company, and its executive officers and directors, and indemnification of the underwriters by the Company for certain liabilities, including liabilities arising under the Securities Act of 1933, as amended, in connection with matters specifically provided in writing by the underwriters for inclusion in the registration statement.

The Company intends to purchase and maintain insurance on behalf of any person who is or was a director or officer against any loss arising from any claim asserted against him or her and incurred by him or her in that capacity, subject to certain exclusions and limits of the amount of coverage.

**Item 15. Recent Sales of Unregistered Securities**

In the three years preceding the filing of this registration statement, we have issued the following securities that were not registered under the Securities Act:

**Issuances of Capital Stock**

On February 15, 2011, we issued an aggregate of 2,682,011 shares of our Series B redeemable convertible preferred stock to three investors for aggregate consideration of \$2,024,999.

On June 30, 2011, we issued an aggregate of 6,716,624 shares of our Series C redeemable convertible preferred stock to six investors for aggregate consideration of \$6,085,933. On December 1, 2011, we issued an aggregate of 2,207,260 of our Series C redeemable convertible preferred stock to two investors for aggregate consideration of \$1,999,998. On February 1, 2012, we issued an aggregate of 7,808,400 shares of our Series C redeemable convertible preferred stock to six investors for aggregate consideration of \$7,075,191.

On August 13, 2012 and November 8, 2012, we issued convertible promissory notes to two of our existing investors for an aggregate principal amount of \$6,000,000. On November 30, 2012, we issued an aggregate of 4,975,260 shares of our Series D redeemable convertible preferred stock to such investors upon conversion of the notes.



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On November 30, 2012, we issued an aggregate of 6,653,988 shares of our Series D redeemable convertible preferred stock to four investors for aggregate consideration of \$9,044,101 in cash. On January 11, 2013, we issued an aggregate of 4,381,914 shares of our Series D redeemable convertible preferred stock to two investors for aggregate consideration of \$5,955,898.

On November 25, 2013, we issued an aggregate of 16,110,473 shares of our Series E redeemable convertible preferred stock to eight investors for aggregate consideration of \$35,000,002 in cash.

On February 28, 2014, we issued an aggregate of 204,101 shares of at Series E redeemable convertible preferred stock to four investors for aggregate consideration of \$443,409 in cash.

No underwriters were used in the foregoing transactions. All sales of securities described above were made in reliance upon the exemption from registration provided by Section 4(2) of the Securities Act (and/or Regulation D promulgated thereunder) for transactions by an issuer not involving a public offering. All of the foregoing securities are deemed restricted securities for the purposes of the Securities Act.

### **Grants of Stock Options**

Since January 1, 2011, we have granted stock options to purchase an aggregate of 8,827,748 shares of our common stock, with exercise prices ranging from \$0.25 to \$1.54 per share, to employees, directors and consultants pursuant to our stock option plan. The issuances of these securities were exempt either pursuant to Rule 701, as a transaction pursuant to a compensatory benefit plan, or pursuant to Section 4(2), as a transaction by an issuer not involving a public offering.

### **Item 16. Exhibits and Financial Statement Schedules**

#### **(a) Exhibits.**

The exhibits to the registration statement are listed in the Exhibit Index to this registration statement and are incorporated herein by reference.

#### **(b) Financial Statement Schedules.**

None.

### **Item 17. Undertakings**

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

(a) The undersigned Registrant will provide to the underwriters at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

(b) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form

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of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(c) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on the 28<sup>th</sup> day of April, 2014.

ZAFGEN, INC.

By: /s/ Thomas E. Hughes

Thomas E. Hughes, Ph.D.  
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities indicated below on the 28<sup>th</sup> day of April, 2014.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Thomas E. Hughes</u> THOMAS E. HUGHES, PH.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	April 28, 2014
<u>/s/ Patricia L. Allen</u> PATRICIA L. ALLEN	Chief Financial Officer (Principal Financial and Accounting Officer)	April 28, 2014
<u>*</u> PETER BARRETT, PH.D.	Chairman of the Board of Directors	April 28, 2014
<u>*</u> BRUCE BOOTH, PH.D.	Director	April 28, 2014
<u>*</u> AVI GOLDBERG	Director	April 28, 2014
<u>*</u> JOHN L. LAMATTINA, PH.D.	Director	April 28, 2014
<u>*</u> KEVIN P. STARR	Director	April 28, 2014
<u>*</u> LOU TARTAGLIA, PH.D.	Director	April 28, 2014

\* Pursuant to Power of Attorney

By: /s/ Thomas E. Hughes  
THOMAS E. HUGHES, PH.D.

**EXHIBIT INDEX**

<u>Exhibit No.</u>	<u>Description</u>
1.1*	Form of Underwriting Agreement
3.1**	Seventh Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect
3.2*	Form of Amended and Restated Certificate of Incorporation of the Registrant, to be in effect upon completion of the offering
3.3**	Second Amended and Restated By-laws of the Registrant and the amendments thereto, as currently in effect
3.4*	Form of Amended and Restated By-laws of the Registrant, to be in effect upon completion of the offering
4.1*	Specimen Common Stock Certificate
4.2**	Third Amended and Restated Investors' Rights Agreement by and among the Registrant and certain of its stockholders dated November 25, 2013
5.1*	Opinion of Goodwin Procter LLP
10.1**#	Amended and Restated 2006 Stock Option Plan and forms of award agreements thereunder
10.2**#	2014 Stock Option and Incentive Plan and forms of award agreements thereunder
10.3**†	Exclusive License Agreement by and between the Registrant and Chong Kun Dang Pharmaceutical Corp. of South Korea, dated July 6, 2009, as amended
10.4**	Lease Agreement by and between the Company and MIT One Broadway LLC, dated July 8, 2011, as amended by First Amendment to Lease, dated June 20, 2013
10.5**	Letter by and between the Registrant and Thomas E. Hughes, dated July 25, 2008
10.6**	Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement by and between the Registrant and Thomas E. Hughes, dated July 29, 2008
10.7**	Letter by and between the Registrant and Dennis D. Kim, dated August 23, 2011
10.8**	Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement by and between the Registrant and Dennis D. Kim, dated August 29, 2013
10.9**	Letter by and between the Registrant and Patricia L. Allen, dated December 10, 2012
10.10**	Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement by and between the Registrant and Patricia L. Allen, dated August 29, 2013
10.11*	Form of Indemnification Agreement, to be entered into between the Registrant and its officers and directors
10.12**#	Senior Executive Cash Incentive Bonus Plan
10.13**†	Exclusive License Agreement by and between the Registrant and Children's Medical Center Corporation, dated January 4, 2007, as amended January 15, 2007
21.1**	Subsidiaries of the Registrant
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
23.2*	Consent of Goodwin Procter LLP (included in Exhibit 5.1)
24.1**	Power of Attorney (included on signature page)

\* To be filed by amendment.

\*\* Previously filed.

† Application has been made to the Securities and Exchange Commission for confidential treatment of certain provisions. Omitted material for which confidential treatment has been requested has been filed separately with the Securities and Exchange Commission.

# Represents management compensation plan.

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the use in this Amendment No. 1 to the Registration Statement on Form S-1 of Zafgen, Inc. of our report dated March 14, 2014 relating to the consolidated financial statements of Zafgen, Inc., which appears in such Registration Statement. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts  
April 28, 2014