

Edgar Filing: Atara Biotherapeutics, Inc. - Form S-1/A

Atara Biotherapeutics, Inc.  
Form S-1/A  
July 09, 2015  
Table of Contents

As filed with the Securities and Exchange Commission on July 9, 2015.

Registration No. 333-205347

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

**AMENDMENT NO. 2**  
**TO**  
**FORM S-1**  
**REGISTRATION STATEMENT**  
*UNDER*  
*THE SECURITIES ACT OF 1933*

**ATARA BIOTHERAPEUTICS, INC.**

(Exact name of Registrant as specified in its charter)

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Delaware  
(State or other jurisdiction of  
incorporation or organization)

2836  
(Primary Standard Industrial  
Classification Code Number)  
701 Gateway Blvd., Suite 200

46-0920988  
(I.R.S. Employer  
Identification Number)

South San Francisco, California 94080

(650) 278-8930

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

Isaac E. Ciechanover, M.D.

Chief Executive Officer

Atara Biotherapeutics, Inc.

701 Gateway Blvd., Suite 200

South San Francisco, California 94080

(650) 278-8930

(Name, address, including zip code and telephone number, including area code, of agent for service)

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**Approximate date of commencement of proposed sale to the public:** As soon as practicable after the effective date of this registration statement.

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, check the following box. "

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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

	<b>Proposed maximum aggregate offering price<sup>(1)(2)</sup></b>	<b>Amount of registration fee<sup>(3)</sup></b>
Common Stock, par value \$0.0001 per share	\$172,500,000	\$20,045

- (1) Includes the offering price of any additional shares that the underwriters have the option to purchase from the Registrant.
- (2) Estimated solely for the purpose of computing the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended (the Securities Act ).
- (3) The Registrant previously paid a total of \$16,704 in connection with the initial filing of the registration statement. In accordance with Rule 457(a) under the Securities Act, an additional registration fee of \$3,341 is being paid with this amendment to the registration statement.

**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, as amended, or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission acting pursuant to said Section 8(a), may determine.**

**Table of Contents**

**The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.**

**Subject to Completion. Dated July 9, 2015.**

**\$150,000,000**

**Common Stock**

We are offering \$150,000,000 of shares of our common stock or, assuming a public offering price of \$48.83 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on July 8, 2015, 3,071,882 shares of our common stock. Our common stock is listed on The Nasdaq Global Select Market under the symbol ATRA.

We are an emerging growth company under applicable Securities and Exchange Commission rules and are subject to reduced public company reporting requirements.

*Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page 12 to read about factors you should consider before buying shares of our common stock.*

**Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.**

	Per Share	Total
Public offering price	\$	\$
Underwriting discounts and commissions <sup>(1)</sup>	\$	\$
Proceeds to us, before expenses	\$	\$

(1) We refer you to Underwriting beginning on page 131 for additional information regarding total underwriting compensation. We have granted the underwriters an option to purchase up to an additional \$22,500,000 of shares of common stock at the public offering price, less underwriting discounts and commissions.

The underwriters expect to deliver the shares against payment in New York, New York on \_\_\_\_\_, 2015.

**Goldman, Sachs & Co.**

**Citigroup**

**William Blair**

**Canaccord Genuity**

**JMP Securities**

Prospectus dated \_\_\_\_\_, 2015

**Table of Contents****TABLE OF CONTENTS**

	<b>Page</b>
<u>Prospectus Summary</u>	1
<u>Summary Consolidated and Combined Financial Data</u>	10
<u>Risk Factors</u>	12
<u>Special Note Regarding Forward-Looking Statements and Industry Data</u>	52
<u>Use of Proceeds</u>	54
<u>Market Price of Common Stock</u>	55
<u>Dividend Policy</u>	56
<u>Capitalization</u>	57
<u>Dilution</u>	58
<u>Business</u>	59
<u>Certain Relationships and Related Person Transactions</u>	113
<u>Principal Stockholders</u>	117
<u>Description of Capital Stock</u>	120
<u>Shares Eligible for Future Sale</u>	125
<u>Material US Federal Income Tax Consequences to Non-US Holders of Our Common Stock</u>	127
<u>Underwriting</u>	131
<u>Legal Matters</u>	137
<u>Experts</u>	137
<u>Where You Can Find More Information</u>	137
<u>Incorporation of Certain Information by Reference</u>	138

We have not authorized anyone to provide you with any information or to make any representation, other than those contained or incorporated by reference in this prospectus or in any free writing prospectus we have prepared. We take no responsibility for, and provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only in circumstances and in jurisdictions where it is lawful to do so. The information contained or incorporated by reference in this prospectus is accurate only as of its date, regardless of the time of delivery of this prospectus or of any sale of our common stock.

Neither we nor any of the underwriters have 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. You are required to inform yourself about, and to observe any restrictions relating to, this offering and the distribution of this prospectus.

Atara, Atara Biotherapeutics, the Atara logo and other trade names, trademarks or service marks of Atara appearing in this prospectus are the property of Atara. Trade names, trademarks and service marks of other companies appearing in this prospectus are the property of their respective holders.

**Table of Contents**

**PROSPECTUS SUMMARY**

*This summary highlights information contained or incorporated by reference 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 read the entire prospectus carefully, including the section titled *Risk Factors* and the information in our filings with the Securities and Exchange Commission, or SEC, incorporated by reference in this prospectus. Unless the context suggests otherwise, references in this prospectus to Atara, Atara Biotherapeutics, we, us and our refer to Atara Biotherapeutics, Inc. and, where appropriate, its subsidiaries.*

**Atara Biotherapeutics, Inc.**

We are a clinical-stage biopharmaceutical company focused on developing novel therapeutics for serious unmet medical needs, with an initial focus on muscle wasting conditions, oncology and viral-associated diseases. We have two groups of product candidates: molecularly targeted biologics and allogeneic, or third-party derived, antigen-specific T-cells, a type of white blood cell. Our molecularly targeted product candidates are biologics that inhibit myostatin and activin, members of the Transforming Growth Factor-Beta, or TGF- $\beta$ , protein superfamily, which play roles in the growth and maintenance of muscle and many other body tissues. Our lead molecularly targeted product candidate, PINTA 745, is in a Phase 2 clinical trial for protein energy wasting, a condition affecting many end-stage renal disease patients. Our second molecularly targeted product candidate is STM 434. We commenced a Phase 1 clinical study of STM 434 for ovarian cancer and other solid tumors in 2014. We have five additional molecularly targeted product candidates that modulate the TGF- $\beta$  pathway in preclinical development. Our T-cell product candidates arise from a platform technology designed to produce off-the-shelf, partially human leukocyte antigen matched cellular therapeutics. We licensed these product candidates from Memorial Sloan Kettering Cancer Center, or MSK, in June 2015. Our initial T-cell product candidates target viral- or cancer-specific antigens and are designed to harness the body's immune system to counteract specific viral infections and cancers. Our most advanced T-cell product candidate, EBV-CTL, is in Phase 2 clinical trials for malignancies associated with Epstein-Barr Virus, including EBV-associated lymphoproliferative diseases, or EBV-LPD. EBV-LPD is a cancer affecting some patients who have received an allogeneic hematopoietic cell transplant, or HCT, or a solid organ transplant, or SOT, or are otherwise immunocompromised. In February 2015, the US Food and Drug Administration, or the FDA, granted Breakthrough Therapy designation for EBV-CTL in the treatment of rituximab-refractory EBV-LPD after HCT, commonly known as bone marrow transplant. Our second T-cell product candidate, CMV-CTL, is in Phase 2 clinical trials for cytomegalovirus, or CMV, an infection that occurs in some patients who have received an HCT, SOT, or are otherwise immunocompromised. Our third T-cell product candidate, WT1-CTL, targets cancers expressing the antigen Wilms Tumor 1 and is currently in Phase 1 clinical studies.

***Our Novel Approach to Treat Protein Energy Wasting in ESRD Patients: PINTA 745***

Our lead molecularly targeted product candidate, PINTA 745, is a peptibody that binds to and inhibits myostatin, a protein that down regulates muscle growth and maintenance. In a Phase 1 study, PINTA 745 was found to increase muscle mass compared to placebo after one month of weekly dosing, an increase that was statistically significant, indicating that it is more likely than not that the benefit observed in the study was due to drug treatment rather than chance. We are enrolling a US-based Phase 2 clinical trial to further establish the role of PINTA 745 in building muscle mass, as well as to collect data from corresponding functional muscle tests. This trial is being conducted in patients with end-stage renal disease, or ESRD, who are also suffering from protein-energy wasting, or PEW, a condition characterized by muscle wasting, inflammation and malnutrition.

## **Table of Contents**

PEW is a major complication of ESRD. A recent study we completed with DaVita Clinical Research, a division of DaVita Healthcare Partners Inc., concluded that more than half of the patients in DaVita's dialysis population met the conditions for PEW and, in comparison to the rest of the group, exhibited worse morbidity and mortality. Based on data from the US Renal Data System, we estimate that the current total US dialysis population, excluding patients who had successfully received kidney transplants, is 460,000 patients. Of these patients, we estimate that approximately 250,000 patients suffer from PEW. Worldwide, we believe that more than 800,000 patients suffer from PEW.

There is currently no approved therapy for patients suffering from PEW. We believe PINTA 745 is the only therapeutic in clinical development to treat this patient population.

In clinical studies conducted of PINTA 745 in men with prostate cancer and in mouse studies in a model of chronic kidney disease, or CKD, conducted with PINTA 745/s, a version of PINTA 745 that was customized for use in mice, several properties well suited for a potential therapeutic for PEW were observed, including:

***Reversing muscle loss*** PINTA 745 not only stopped muscle wasting, it significantly increased muscle mass after four weeks of treatment.

***Anti-inflammatory properties*** In an animal model of renal disease, PINTA 745/s exhibited significant anti-inflammatory properties, a factor that we believe will be important due to the critical role that inflammation plays in PEW and the overall declining health of ESRD patients.

***Dosing schedule*** PINTA 745 is dosed weekly, which conveniently aligns with dialysis treatment schedules.

Our ongoing US-based Phase 2 trial is a 48-patient, randomized, double-blind, placebo-controlled trial that, in addition to providing us with assessments of change in muscle mass and muscle strength, will give us insight into potential additional markets for PINTA 745. These could include: orthopedic indications; inflammation and inflammatory diseases; age-related sarcopenia, or loss of muscle; and cancer cachexia, a syndrome of progressive weight loss. In each of these conditions, muscle loss prevention, muscle growth and reduction in inflammation resulting from treatment with PINTA 745 could lead to improved physical function and therefore better outcomes. As of June 30, 2015, we had enrolled 34 of the planned 48 patients, and we expect to release preliminary top-line data from this Phase 2 clinical trial in the fourth quarter of 2015.

### ***Our Novel Approach to Treat Ovarian Cancer: STM 434***

Our second molecularly targeted product candidate, STM 434, is in a Phase 1 clinical study that will enroll approximately 66 patients with ovarian cancer and other solid tumors. STM 434 is a soluble ActR2B receptor that binds Activin A. Activin has been shown to be involved in the growth and proliferation of ovarian cancer and other tumors, with published evidence of its role at both the genetic, or messenger RNA, and protein levels. Activin expression is one of a few biomarkers associated with larger tumor volume and poorer outcomes, including shortened survival, in a variety of tumors including ovarian tumors. Published data has shown that serum Activin A levels in ovarian cancer subjects are elevated in relation to levels in normal subjects. We are testing the potential use of Activin A as a biomarker in our Phase 1 clinical study.

Ovarian cancer is the fifth leading cause of cancer death in women in the United States. According to the National Cancer Institute, there were an estimated 22,240 new ovarian cancer cases and 14,030 ovarian cancer deaths in the United States in 2013. Surgery and cytotoxic chemotherapies are widely used to treat ovarian cancer; however, the outcomes have changed little in 40 years. The



## **Table of Contents**

proportion of all ovarian cancer patients surviving five years after diagnosis was only 44% based on the National Cancer Institute SEER database for women diagnosed from 2003 to 2009.

Some subtypes of ovarian tumors respond even more poorly to treatment than others and represent opportunities where drug development could be accelerated. In particular, clear cell and granulosa cell tumors are considered resistant to chemotherapy. Our preclinical experiments in animal models of these subtypes indicate that binding Activin A with a soluble receptor could significantly reduce tumor proliferation, reduce tumor volume and potentially increase survival. We believe that novel therapies for clear cell and granulosa cell tumors could qualify for Breakthrough Therapy designation, an FDA process designed to accelerate the development and review of drugs intended to treat a serious condition when early studies show that the drug may be substantially better than current treatment. Based on its mechanism of action, we also believe that STM 434 has the potential to be the first product to target tumor growth and proliferation through the inhibition of Activin A.

Both PINTA 745 and STM 434 are novel molecules with well-characterized mechanisms of action. They were developed initially, along with our five other in-licensed molecularly targeted biologic programs, at Amgen Inc., or Amgen. Taken together, we believe these unique product candidates constitute a pipeline of biologics that have benefited from years of investment, resulting in a large patent portfolio, broad preclinical testing and, in the case of PINTA 745, promising clinical results. We are evaluating the remaining five product candidates to determine the best path forward. Where appropriate, we intend to conduct preclinical studies and file investigational new drug applications, or INDs, with the FDA for these candidates. For example, we are conducting IND-enabling manufacturing and preclinical studies for ATA 842, a humanized antibody targeting myostatin.

### ***T-Cell Therapy for Cancer and Viral-Associated Diseases: MSK T-Cell Programs***

T-cells are a critical component of the body's immune system and can be harnessed to counteract viral infections and some cancers. By focusing the T-cells on specific proteins involved in cancers and infections, the power of the immune system can be employed to combat these diseases. In June 2015, we exclusively licensed from MSK worldwide rights to three clinical stage T-cell product candidates. We also have an exclusive option to exclusively license from MSK worldwide rights to certain other T-cell programs that are discovered or developed by MSK pursuant to sponsored research funded by us.

Our most advanced T-cell product candidate, EBV-CTL, is in Phase 2 clinical trials for the treatment of EBV-associated malignancies. EBV is the virus that causes mononucleosis and is associated with a number of more severe diseases, including certain malignancies and neurologic conditions, such as multiple sclerosis. EBV-CTL received Breakthrough Therapy designation from the FDA in February 2015 for the treatment of patients with rituximab-refractory EBV-LPD after HCT, based on data from two separate clinical trials conducted by MSK. We recently met with the FDA to discuss late-stage development to support a potential approval in this indication. Based on guidance from the FDA, we intend to conduct a pivotal study in rituximab-refractory EBV-LPD after HCT and expect to submit a special protocol assessment for this pivotal study. In addition, we had preliminary discussions with the FDA regarding late-stage development in the setting of rituximab-refractory EBV-LPD after SOT, and we will be incorporating this feedback into our subsequent development plans in this indication.

Our second T-cell product candidate, CMV-CTL, targets cytomegalovirus. CMV infection can result in blindness, illness or death, depending on the tissue it affects in those with weakened immune systems. CMV is also associated with certain malignancies, including glioblastoma multiforme, or GBM. CMV-CTL is currently being investigated in Phase 2 clinical trials sponsored and conducted by MSK for CMV infections that occur in some patients who have received an HCT.

**Table of Contents**

Our third clinical stage T-cell product candidate, WT1-CTL, targets Wilms Tumor 1, or WT1. Abnormal expression of WT1 is seen in a variety of hematologic and solid tumors, including multiple myeloma, acute myeloid leukemia and ovarian cancer. This product candidate is currently in Phase 1 clinical trials sponsored and conducted by MSK.

Clinical experience with our T-cell product candidates is broad, including in immunocompromised states, as well as in solid and hematologic malignancies. Selected data from clinical studies of our three T-cell product candidates are summarized in the table below.

T-Cell Program	Stage	Indication	Recent Clinical Data Highlights	Number of Patients Who Received Prior Therapy	Historical Outcomes Data
EBV-CTL	Phase 2 clinical trials	EBV lymphoma (EBV-LPD) following allogeneic hematopoietic cell transplantation (HCT) from bone marrow or cord blood	62% response rate in 26 patients treated with EBV-CTL derived from primary HCT donors with 16 complete responses (CR) and zero partial responses (PR) 65% response rate in 34 patients treated with EBV-CTL derived from third-party donor, with 19 CR and three PRs; one-year overall survival (OS) range 56.3-71.8%;	13 of 26 received prior rituximab  All received prior rituximab	Historical median survival in rituximab-refractory patients is 16-56 days
		EBV-LPD following solid organ transplantation (SOT)	two-year OS range 46.9-63.8% 62% response rate in 13 patients treated with third-party derived EBV-CTL with one CR, seven PRs;	All received prior rituximab; 11 of 13 had received prior chemotherapy; 12 of 13 patients had high risk disease	Historical data show 33% OS at two years in patients with incomplete response to rituximab
CMV-CTL	Phase 2 clinical trials	Post-HCT antiviral drug resistant CMV viremia (high viral count) and symptomatic CMV disease	two-year OS of 57.7% 64% response rate in 25 CMV viremia patients treated with third-party derived CMV-CTL, with nine CRs and seven PRs; 67% response rate in nine CMV disease patients, with five CRs and one PR	All received prior antiviral therapy; median of four prior therapies including experimental therapies	Uncontrolled CMV disease leads to high rates of morbidity and mortality (for example, CMV pneumonitis confers a four-fold higher risk of death)
WT1-CTL	Phase 1 clinical studies	Various cancers, including acute myeloid leukemia (AML), multiple myeloma	Data not yet available	Not Applicable	Not Applicable



## **Table of Contents**

We are focusing our initial development and regulatory activities on EBV-CTL in the post-HCT and post-SOT setting and CMV-CTL in the post-HCT setting, rare conditions which we believe offer a rapid path to marketing approvals, if supported by additional clinical data. However, we intend to explore the clinical utility of our T-cell product candidates in other more prevalent disease states.

We anticipate that our T-cell technology platform will have utility beyond the current set of targets to which it has been directed. We and MSK have agreed to collaborate on further research to develop additional cellular therapies, which may include T-cell programs targeted against other antigens and chimeric antigen receptor, or CAR-T cell programs, and which we have an option to license. For example, we may develop cellular therapies with MSK or others directed towards other viral targets such as human papilloma virus, or HPV, which is associated with cervical cancer, anal cancer, and head and neck cancer, and John Cunningham virus, which causes progressive multifocal leukoencephalopathy and is associated with a subset of solid tumors. We also intend to license or acquire additional product candidates or technologies to enhance our existing T-cell technology platform.

### ***Our Management Team***

We believe our management team has the breadth and depth of experience to execute our business model. Our management team includes:

***Isaac E. Ciechanover, M.D.***, our President and Chief Executive Officer, was Executive Director for Business Development at Celgene Corporation, or Celgene. At Celgene, he led the company's venture capital efforts and led licensing and acquisition activities with an aggregate transaction value of more than \$6.7 billion. Prior to founding Atara, Dr. Ciechanover was a Partner with Kleiner Perkins Caufield & Byers, a leading venture capital firm.

***Christopher Haqq, M.D., Ph.D.***, our Chief Medical Officer, was Vice President for Clinical Research and Development at Cougar Biotechnology, Inc., or Cougar Biotechnology, which was acquired by Johnson & Johnson in 2009. At Cougar Biotechnology, he was the lead clinician for a pivotal prostate cancer study leading to market approval for Zytiga (abiraterone acetate). He has served as medical monitor for more than ten clinical trials and served as an attending oncology physician and director of a translational laboratory at the University of California, San Francisco.

***Mitchell G. Clark***, our Chief Regulatory and Quality Officer, was previously Senior Vice President of Global Regulatory Affairs at Abraxis Bioscience, Inc., or Abraxis, where he submitted and managed five INDs for oncology and cardiovascular drugs including Abraxane.

***Gad Soffer***, our Chief Operating Officer, previously held various roles at Celgene, including most recently Global Project Leader for Abraxane following Celgene's acquisition of Abraxis, where he led successful regulatory submissions for pancreatic cancer and non-small cell lung cancer.

***John F. McGrath, Jr.***, our Chief Financial Officer, was previously Executive in Residence and Operating Partner at Kleiner Perkins Caufield & Byers. Prior to that time, he served as Vice President and Chief Financial Officer for Network Equipment Technologies, Inc., a publicly traded company.

## **Table of Contents**

### **Our Strategy**

Our business model is to license or acquire and develop novel therapeutics for serious unmet medical needs with validated targets and established proof of concept. Based on the properties of each of these molecules, including efficacy, safety, pharmacokinetics, affinity and other characteristics, we match each program to clinical indications that we believe maximize its therapeutic potential and may result in an expedited path to market.

Our goal is to be a leader in the development and commercialization of novel therapeutics for serious unmet medical needs. We are initially focused on muscle wasting conditions, oncology and viral-associated diseases. Key components of our strategy to achieve this objective include:

rapidly advance PINTA 745 in clinical development, initially for PEW;

obtain clinical proof of concept for STM 434, initially for ovarian cancer and other solid tumors;

evaluate our other molecularly targeted product candidates and advance them into the clinic as appropriate;

rapidly advance EBV-CTL in clinical development for the treatment of EBV-LPD after HCT or SOT;

develop CMV-CTL based on existing clinical proof of concept data in refractory CMV infection after HCT;

continue development of WT1-CTL and collaborate with MSK in the discovery and development of additional T-cell programs; and

leverage our relationships and experience to in-license or acquire additional product candidates for development.

### **Risks Associated with Our Business**

Our business is subject to numerous risks and uncertainties, including those highlighted in the section titled "Risk Factors" immediately following this prospectus summary. Some of these risks are:

we have a limited operating history on which to assess our business, have generated no revenues, have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future;

we expect that we will need to raise additional financing to achieve our product candidate development, regulatory approval and commercialization goals;

we are very early in our product candidate development efforts and are heavily dependent on the regulatory approval and successful commercialization of our product candidates;

our T-cell product candidates represent new therapeutic approaches that present significant challenges;

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we rely on third parties to conduct our preclinical studies and clinical trials;

we have no experience manufacturing our product candidates on a large clinical or commercial scale and are dependent on third parties to conduct such manufacturing;

our commercial success depends on attaining significant market acceptance of our product candidates, if approved, among physicians, patients, healthcare payors and major operators of dialysis and cancer centers;

**Table of Contents**

if we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, we may not be able to compete effectively; and

our future success depends in part upon our ability to retain members of our executive management team and to attract, retain and motivate other qualified personnel.

**Corporate Information**

We were incorporated in August 2012 in Delaware. Our principal executive offices are located at 701 Gateway Blvd., Suite 200, South San Francisco, California 94080 and our telephone number is (650) 278-8930. Our website address is [www.atarabio.com](http://www.atarabio.com). Information contained on or accessible through our website is not a part of this prospectus and should not be relied upon in determining whether to make an investment decision.

We are an emerging growth company as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, and therefore we may take advantage of certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments. We may take advantage of these exemptions until we are no longer an emerging growth company. We will remain an emerging growth company for up to five years. We will cease to be an emerging growth company upon the earliest of: (1) December 31, 2019; (2) the last day of the first fiscal year in which our annual gross revenues are \$1 billion or more; (3) the date on which we have, during the previous rolling three-year period, issued more than \$1 billion in nonconvertible debt securities; and (4) the date on which we are deemed to be a large accelerated filer as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act. We have chosen to irrevocably opt out of the extended transition periods available under the JOBS Act for complying with new or revised accounting standards.

**Table of Contents**

**The Offering**

Common stock offered by Atara 3,071,882 shares

Option to purchase additional shares of common stock 460,782 shares

Common stock to be outstanding after this offering 27,432,129 shares

Use of proceeds We estimate that our net proceeds from this offering will be approximately \$140.4 million, or approximately \$161.5 million if the underwriters' option to purchase additional shares of our common stock is exercised in full, after deducting underwriting discounts and commissions and estimated offering expenses.

We intend to use the net proceeds from this offering, along with our other capital resources, primarily (1) to complete our planned confirmatory Phase 2 clinical trial of PINTA 745, (2) to continue our initial Phase 1 clinical study of STM 434, (3) to continue the ongoing and planned studies and trials with our T-cell product candidates and (4) to continue to expand and advance our clinical and preclinical pipeline for working capital and for other general corporate purposes and to potentially acquire or license other product candidates, businesses or technologies, although we have no present commitments for any such acquisitions or licenses. See "Use of Proceeds" for additional information.

Risk factors See "Risk Factors" beginning on page 12 and the other information included in, or incorporated by reference into, this prospectus for a discussion of factors you should carefully consider before deciding to invest in our common stock.

Nasdaq Global Select Market symbol ATRA

The number of shares of common stock to be outstanding after this offering is based on 24,360,247 shares of our common stock outstanding as of March 31, 2015, and excludes the following:

906,391 shares of common stock issuable upon settlement of restricted stock units, or RSUs, outstanding as of March 31, 2015;

1,314,635 shares of common stock issuable upon the exercise of options outstanding as of March 31, 2015 with a weighted average exercise price of \$19.61 per share;

2,046,541 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, or 2014 Plan as of March 31, 2015;





**Table of Contents**

432,898 shares of common stock reserved for issuance under our 2014 Employee Stock Purchase Plan, or our ESPP, as of March 31, 2015; and

any future automatic increases in the number of shares of common stock reserved for issuance under our 2014 Plan or ESPP.

In addition, unless we specifically state otherwise, all information in this prospectus assumes no exercise of the underwriters' option to purchase up to an additional 460,782 shares of common stock from us.

**Table of Contents****SUMMARY CONSOLIDATED AND COMBINED FINANCIAL DATA**

The following tables summarize our consolidated and combined financial data. You should read this summary consolidated and combined financial data together with the sections titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K and our Quarterly Report on Form 10-Q, our consolidated and combined financial statements and related notes, each of which is incorporated by reference in this prospectus.

We have derived the summary combined statement of operations data for the years ended December 31, 2013 and 2014 from our audited consolidated and combined financial statements. We have derived the summary consolidated and combined statements of operations data for the three months ended March 31, 2014 and 2015 and our consolidated balance sheet data as of March 31, 2015 from our unaudited interim consolidated and combined financial statements. The unaudited interim consolidated and combined financial statements have been prepared on the same basis as the audited consolidated and combined financial statements and reflect, in the opinion of management, all adjustments of a normal, recurring nature that are necessary for a fair presentation of the unaudited interim consolidated and combined financial statements. Our historical results are not necessarily indicative of the results that should be expected in the future, and our interim results are not necessarily indicative of the results that should be expected for the full year or any other period.

	<b>Year ended December 31,</b>		<b>Three months ended March 31,</b>	
	<b>2013</b>	<b>2014</b>	<b>2014</b>	<b>2015</b>
	<b>(In thousands, except per share information)</b>			
<i>Consolidated and Combined Statements of Income Data</i>				
<b>Operating Expenses:</b>				
Research and development	\$ 4,306	\$ 14,380	\$ 2,981	\$ 5,767
Research and development costs paid to Amgen	553	1,066		
General and administrative	3,756	12,710	4,096	3,544
<b>Total operating expenses</b>	<b>8,615</b>	<b>28,156</b>	<b>7,077</b>	<b>9,311</b>
Loss from operations	(8,615)	(28,156)	(7,077)	(9,311)
Interest and other income	12	125	6	153
Loss before provision for income taxes	(8,603)	(28,031)	(7,071)	(9,158)
Provision (benefit) for income taxes	170	(25)	(22)	2
Net loss	\$ (8,773)	\$ (28,006)	\$ (7,049)	\$ (9,160)
<b>Comprehensive loss</b>	<b>\$ (8,773)</b>	<b>\$ (28,106)</b>	<b>\$ (7,060)</b>	<b>\$ (9,078)</b>
Basic and diluted net loss per common share <sup>(1)</sup>	\$ (9.08)	\$ (5.62)	\$ (5.58)	\$ (0.42)

(1) Periods presented prior to our October 2014 initial public offering do not give effect to the automatic conversion of our preferred stock into common stock upon the closing of our initial public offering.

**Table of Contents**

	As of March 31, 2015	
	Actual	As Adjusted <sup>(1)</sup>
	(In thousands)	
<i>Consolidated and Combined Balance Sheet Data</i>		
Cash, cash equivalents and investments	\$ 166,696	\$ 307,046
Working capital	\$ 166,177	\$ 306,527
Total assets	\$ 169,817	\$ 310,167
Total stockholders' equity	\$ 166,094	\$ 306,444

- (1) The as adjusted column reflects the sale of 3,071,882 shares of our common stock in this offering, at the assumed public offering price of \$48.83 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on July 8, 2015, after deducting underwriting discounts and commissions and estimated offering expenses. The as adjusted column does not reflect our \$4.5 million obligation to MSK, incurred in June 2015 in connection with the exercise of our option to license certain T-cell product candidates from MSK.

**Table of Contents**

**RISK FACTORS**

*Investing in our common stock involves a high degree of risk. You should carefully consider the following risks and all of the other information included and incorporated by reference in this prospectus before investing in our common stock. While we believe that the risks and uncertainties described below are the material risks currently facing us, additional risks that we do not yet know of or that we currently think are immaterial may also arise and materially affect our business. If any of the following risks materialize, our business, financial condition and results of operations could be materially and adversely affected. In that case, the trading price of our common stock could decline, and you may lose some or all of your investment.*

**Risks Related to Our Financial Results and Capital Needs**

*We have incurred substantial losses since our inception and anticipate that we will continue to incur substantial and increasing losses for the foreseeable future.*

We are a clinical-stage biopharmaceutical company. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a product candidate will fail to prove effective, gain regulatory approval or become commercially viable. We do not have any products approved by regulatory authorities and have not generated any revenues from product sales to date, and have incurred significant research, development and other expenses related to our ongoing operations and expect to continue to incur such expenses. As a result, we have not been profitable and have incurred significant operating losses in every reporting period since our inception. For the year ended December 31, 2014 and the three months ended March 31, 2015, we reported a net loss of \$28.0 million and \$9.2 million, respectively, and we had an accumulated deficit of \$50.0 million at March 31, 2015.

We do not expect to generate revenues for many years, if at all. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate these losses to increase as we continue to research, develop and seek regulatory approvals for our product candidates and any additional product candidates we may acquire, and potentially begin to commercialize product candidates that may achieve regulatory approval. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. If any of our product candidates fails in clinical trials or does not gain regulatory approval, or if approved, fails to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. We anticipate that our expenses will increase in the future as we continue to invest in research and development of our existing product candidates, investigate and potentially acquire new product candidates and expand our manufacturing and commercialization activities.

*We have a limited operating history, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.*

Our company was formed in August 2012. Our operations to date have been limited to organizing and staffing our company, acquiring product and technology rights and conducting product development activities for our product candidates. We have not yet demonstrated our ability to successfully complete any Phase 2 or Phase 3 clinical trials, obtain regulatory approval, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization for any of our product candidates. In addition, the adoptive immunotherapy technology underlying our T-cell product candidates, EBV-CTL,

## **Table of Contents**

CMV-CTL and WT1-CTL, is new and largely unproven. Any predictions about our future success, performance or viability, particularly in view of the rapidly evolving cancer immunotherapy field, may not be as accurate as they could be if we had a longer operating history or approved products on the market.

In addition, as a young business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition. We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

***We currently have no source of revenues. We may never generate revenues or achieve profitability.***

To date, we have not generated any revenues from product sales or otherwise. Even if we are able to successfully achieve regulatory approval for our product candidates, we do not know when we will generate revenues or become profitable, if at all. Our ability to generate revenues from product sales and achieve profitability will depend on our ability to commercialize products, including any of our current product candidates, and other product candidates that we may develop, in-license or acquire in the future. Our ability to generate revenues and achieve profitability also depends on a number of additional factors, including our ability to:

successfully complete development activities, including the necessary clinical trials;

complete and submit biologics license applications, or BLAs, to the FDA and obtain US regulatory approval for indications for which there is a commercial market;

complete and submit applications to, and obtain regulatory approval from, foreign regulatory authorities in Europe, Asia and other jurisdictions;

obtain coverage and adequate reimbursement from third parties, including government and private payors;

set a commercially viable price for our products;

establish and maintain supply and manufacturing relationships with reliable third parties and ensure adequate, legally compliant manufacturing of bulk drug substances and drug products to maintain that supply;

develop manufacturing and distribution processes for our novel T-cell product candidates;

obtain commercial quantities of our products at acceptable cost levels;

achieve market acceptance of our products, if any;

attract, hire and retain qualified personnel;

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protect our rights in our intellectual property portfolio;

develop a commercial organization capable of sales, marketing and distribution for any products we intend to sell ourselves in the markets in which we choose to commercialize on our own; and

find suitable distribution partners to help us market, sell and distribute our approved products in other markets.

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**Table of Contents**

Our revenues for any product candidate for which regulatory approval is obtained will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our addressable disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenues from sales of such products, even if approved. In addition, we anticipate incurring significant costs associated with commercializing any approved product candidate. As a result, even if we generate revenues, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and may be forced to reduce our operations.

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

We expect to expend substantial resources for the foreseeable future continuing the clinical development and manufacturing of PINTA 745, STM 434, EBV-CTL, CMV-CTL and WT1-CTL and the advancement and expansion of our preclinical research pipeline, including ATA 842. These expenditures will include costs associated with research and development, potentially acquiring new product candidates or technologies, conducting preclinical studies and clinical trials and potentially obtaining regulatory approvals and manufacturing products, as well as marketing and selling products approved for sale, if any. Under the terms of our license agreements with Amgen and MSK, we are obligated to make an upfront payment to MSK of \$4.5 million and additional milestone payments of up to \$86.0 million to Amgen and up to \$33.0 million to MSK with respect to the three licensed clinical stage T-cell programs upon the achievement of certain development, regulatory approval or commercial milestones. In addition, other unanticipated costs may arise. Because the design and outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates.

Our future capital requirements depend on many factors, including:

the scope, progress, results and costs of researching and developing our other product candidates, and conducting preclinical studies and clinical trials;

the timing of, and the costs involved in, obtaining regulatory approvals for our other product candidates if clinical trials are successful;

the cost of commercialization activities for our product candidates, if any of these product candidates is approved for sale, including marketing, sales and distribution costs;

the cost of manufacturing our product candidates for clinical trials in preparation for regulatory approval and in preparation for commercialization;

our ability to establish and maintain strategic licensing or other arrangements and the financial terms of such agreements;

the costs to in-license future product candidates or technologies;

the costs involved in preparing, filing, prosecuting, maintaining, expanding, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;

the timing, receipt and amount of sales of, or royalties on, our future products, if any; and



the emergence of competing technologies or other adverse market developments.

## **Table of Contents**

Based on our current operating plan, we believe that our existing cash and cash equivalents and short-term investments, together with the net proceeds from this offering, will be sufficient to fund our projected operating requirements through the second half of 2018. As of March 31, 2015, we had cash and cash equivalents and short-term investments of \$166.7 million. However, our operating plan may change as a result of many factors currently unknown to us, and we may need additional funds sooner than planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. We do not have any committed external source of funds. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more of our product candidates or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates.

***Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product candidates on unfavorable terms to us.***

We may seek additional capital through a variety of means, including through private and public equity offerings and debt financings. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds from third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts for our product candidates, or grant to others the rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. At December 31, 2014, we had federal and state net operating loss, or NOL, carryforwards of approximately \$20.6 million, which, if not utilized, begin to expire in various amounts beginning in the year 2032. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, if over a rolling three-year period, the cumulative change in our ownership exceeds 50% (as determined under applicable Treasury regulations), our ability to utilize our US NOL carryforwards and other pre-change tax attributes (such as research tax credits) to offset future taxable income or taxes may be limited. We have experienced at least one ownership change since inception and our utilization of NOL carryforwards will therefore be subject to annual limitation. Our ability to utilize our NOL carryforwards may be further limited as a result of subsequent ownership changes, including potential changes in connection with this offering. Similar rules may apply under state tax laws. Further, other provisions of the Code may limit our ability to utilize NOLs incurred before the recapitalization to offset income or gain realized after the recapitalization, unless such income or gain is realized by the same entity that originally incurred such NOLs. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited. Such limitations could result in the expiration of our carryforwards before they can be utilized and, if we are profitable, our future cash flows could be adversely affected due to our increased tax liability.

**Table of Contents**

**Risks Related to the Development of Our Product Candidates**

*We are very early in our development efforts and have only five product candidates in clinical development. All of our other product candidates are still in preclinical development. If we or our collaborators are unable to successfully develop and commercialize product candidates or experience significant delays in doing so, our business may be materially harmed.*

We are very early in our development efforts. We have five product candidates, PINTA 745, STM 434, EBV-CTL, CMV-CTL and WT1-CTL, in clinical development. All of our other product candidates are currently in preclinical development. We have invested substantially all of our efforts and financial resources in identifying and developing potential product candidates and conducting preclinical studies, clinical trials and manufacturing activities. Our ability to generate revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates. The success of our product candidates will depend on several factors, including the following:

completion of preclinical studies and clinical trials with positive results;

receipt of regulatory approvals from applicable authorities;

obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;

making arrangements with third-party manufacturers for, or establishing, commercial manufacturing capabilities;

develop manufacturing and distribution processes for our novel T-cell product candidates;

manufacturing products at an acceptable cost;

launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;

acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors;

effectively competing with other therapies;

obtaining and maintaining coverage and adequate reimbursement by third-party payors, including government payors, for our product candidates;

protecting our rights in our intellectual property portfolio;

maintaining a continued acceptable safety profile of the products following approval; and

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maintaining and growing an organization of scientists and business people who can develop and commercialize our products and technology.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully develop and commercialize our product candidates, which could materially harm our business.

***Our future success is dependent on the regulatory approval of our product candidates.***

We do not have any products that have gained regulatory approval. Currently, our only clinical-stage product candidates are PINTA 745, EBV-CTL and CMV-CTL, which are in Phase 2 clinical trials, and STM 434 and WT1-CTL, which are in Phase 1 clinical studies. Our business is substantially dependent on our ability to obtain regulatory approval for, and, if approved, to successfully commercialize our product candidates in a timely manner. We cannot commercialize product candidates in the United States without first obtaining regulatory approval for the product from the FDA;

## **Table of Contents**

similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of any product candidate for a target indication, we must demonstrate with substantial evidence gathered in preclinical and clinical studies, generally including two well-controlled Phase 3 trials, that the product candidate is safe and effective for use for that target indication and that the manufacturing facilities, processes and controls are adequate with respect to such product candidate.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates or any future product candidates will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval from the FDA or a comparable foreign regulatory authority for many reasons, including:

disagreement with the design or implementation of our clinical trials;

failure to demonstrate that a product candidate is safe and effective for its proposed indication;

failure of clinical trials to meet the level of statistical significance required for approval;

failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;

disagreement with our interpretation of data from preclinical studies or clinical trials;

the insufficiency of data collected from clinical trials of our product candidates to support the submission and filing of a BLA or other submission or to obtain regulatory approval;

failure to obtain approval of the manufacturing processes or facilities of third-party manufacturers with whom we contract for clinical and commercial supplies; or

changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or a comparable foreign regulatory authority may require more information, including additional preclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program. If we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request (including failing to approve the most commercially promising indications), may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate.

Even if a product candidate were to successfully obtain approval from the FDA and comparable foreign regulatory authorities, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval study or risk management requirements. If we are unable to obtain regulatory approval for one of our product candidates in one or more jurisdictions, or any approval contains significant limitations, we may not be able to obtain sufficient funding to continue the development of that product or generate revenues attributable to that product candidate. Also, any regulatory approval of our

current or future product candidates, once obtained, may be withdrawn.

**Table of Contents**

*Our T-cell product candidates, EBV-CTL, CMV-CTL and WT1-CTL, represent new therapeutic approaches that present significant challenges.*

Our future success is dependent in part on the successful development of T-cell immunotherapies in general and our EBV-CTL, CMV-CTL and WT1-CTL product candidates in particular. Because these programs represent a new approach to immunotherapy for the treatment of cancer and other diseases, developing and commercializing our product candidates subject us to a number of challenges, including:

obtaining regulatory approval from the FDA and other regulatory authorities, which have very limited experience with the commercial development of T-cell therapies;

developing and deploying consistent and reliable processes for procuring blood from consenting third-party donors, isolating T-cells from the blood of such donors, activating the isolated T-cells against a specific antigen, characterizing and storing the resulting activated T-cells for future therapeutic use, selecting and delivering an appropriate partially HLA matched cell line from among the available T-cell lines, and finally infusing these activated T-cells into patients;

utilizing these product candidates in combination with other therapies, which may increase the risk of adverse side effects;

educating medical personnel regarding the potential side effect profile of each of our product candidates;

developing processes for the safe administration of these products, including long-term follow-up for all patients who receive these product candidates;

sourcing clinical and, if approved, commercial supplies for the materials used to manufacture and process these product candidates;

developing a manufacturing process and distribution network with a cost of goods that allows for an attractive return on investment;

establishing sales and marketing capabilities after obtaining any regulatory approval to gain market acceptance, and obtaining adequate coverage, reimbursement and pricing by third-party payors and government authorities; and

developing therapies for types of diseases beyond those initially addressed by our current product candidates.

We cannot be sure that the manufacturing processes used in connection with our T-cell product candidates, EBV-CTL, CMV-CTL and WT1-CTL, will yield satisfactory products that are safe and effective, scalable or profitable.

Moreover, public perception of therapy safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to subscribe to the novel treatment mechanics. Physicians, hospitals and third-party payors often are slow to adopt new products, technologies and treatment practices that require additional upfront costs and training. Physicians may not be willing to undergo training to adopt this novel therapy, may decide the therapy is too complex to adopt without appropriate training and may choose not to administer the therapy. Based on these and other factors, hospitals and payors may decide that the benefits of this new therapy do not or will not outweigh its costs.

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**Table of Contents**

*The results of preclinical testing or earlier clinical studies are not necessarily predictive of future results. Our existing product candidates in clinical studies or trials, and any other product candidate we advance into clinical studies or trials, may not have favorable results in later clinical studies or trials or receive regulatory approval.*

Success in preclinical studies and early clinical trials does not ensure that later clinical trials will generate adequate data to demonstrate the efficacy and safety of an investigational drug. A number of companies in the pharmaceutical and biotechnology industries, including those with greater resources and experience than us, have suffered significant setbacks in clinical trials, even after seeing promising results in earlier preclinical studies or clinical studies or trials. Despite the results reported in earlier preclinical studies or clinical studies or trials for our product candidates, we do not know whether the clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market PINTA 745, STM 434, EBV-CTL, CMV-CTL or WT1-CTL or any of our other product candidates in any particular jurisdiction. For example, our EBV-CTL, CMV-CTL and WT1-CTL product candidates have only been evaluated in single-center studies under investigator-sponsored INDs held by MSK, and the findings may not be reproducible in multi-center studies conducted under commercially-sponsored INDs. In addition, the Phase 2 clinical trials with EBV-CTL enrolled a heterogeneous group of patients with a variety of EBV-associated malignancies, including but not limited to EBV-LPD after HCT and EBV-LPD after SOT. These Phase 2 studies were not prospectively designed to evaluate the efficacy of EBV-CTL in the treatment of a single disease state for which we may later seek approval. Efficacy data from prospectively designed studies may differ significantly from those obtained from retrospective subgroup analyses. If later-stage clinical trials do not produce favorable results, our ability to achieve regulatory approval for any of our product candidates may be adversely impacted. Even if we believe that we have adequate data to support an application for regulatory approval to market any of our product candidates, the FDA or other regulatory authorities may not agree and may require that we conduct additional clinical trials.

*Clinical drug development involves a lengthy and expensive process with an uncertain outcome.*

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical and clinical studies and early clinical trials.

We may experience delays in our ongoing or future clinical studies or trials and we do not know whether planned clinical studies or trials will begin or enroll subjects on time, will need to be redesigned or will be completed on schedule, if at all. There can be no assurance that the FDA will not put clinical studies or trials of any of our product candidates on clinical hold in the future. Clinical studies or trials may be delayed, suspended or prematurely terminated for a variety of reasons, such as:

delay or failure in reaching agreement with the FDA or a comparable foreign regulatory authority on a study or trial design that we are able to execute;

delay or failure in obtaining authorization to commence a study or trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a study or trial;

delay or failure in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical study or trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and study or trial sites;

delay or failure in obtaining institutional review board, or IRB, approval or the approval of other reviewing entities, including comparable foreign regulatory authorities, to conduct a clinical study or trial at each site;



**Table of Contents**

withdrawal of clinical study or trial sites from our clinical studies or trials or the ineligibility of a site to participate in our clinical studies or trials;

delay or failure in recruiting and enrolling suitable subjects to participate in a study or trial;

delay or failure in subjects completing a study or trial or returning for post-treatment follow-up;

clinical sites and investigators deviating from trial protocol, failing to conduct the study or trial in accordance with regulatory requirements, or dropping out of a study or trial;

inability to identify and maintain a sufficient number of study or trial sites, many of which may already be engaged in other clinical study or trial programs, including some that may be for the same indication;

failure of our third-party clinical study or trial managers to satisfy their contractual duties, meet expected deadlines or return trustworthy data;

delay or failure in adding new study or trial sites;

interim results or data that are ambiguous or negative or are inconsistent with earlier results or data;

feedback from the FDA, the IRB, data safety monitoring boards or a comparable foreign regulatory authority, or results from earlier stage or concurrent preclinical and clinical studies, that might require modification to the protocol for a study or trial;

a decision by the FDA, the IRB, a comparable foreign regulatory authority, or us, or a recommendation by a data safety monitoring board or comparable foreign regulatory authority, to suspend or terminate clinical studies or trials at any time for safety issues or for any other reason;

unacceptable risk-benefit profile, unforeseen safety issues or adverse side effects;

failure to demonstrate a benefit from using a drug;

difficulties in manufacturing or obtaining from third parties sufficient quantities of a product candidate for use in studies or trials;

lack of adequate funding to continue a study or trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional studies or increased expenses associated with the services of our CROs and other third parties; or

changes in governmental regulations or administrative actions or lack of adequate funding to continue a clinical study or trial.

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Patient enrollment, a significant factor in the timing of clinical studies or trials, is affected by many factors including the size and nature of the patient population, the severity of the disease under investigation, the proximity of subjects to clinical sites, the patient referral practices of physicians, the eligibility criteria for the study or trial, the design of the clinical study or trial, ability to obtain and maintain patient consents, risk that enrolled subjects will drop out before completion, competing clinical studies or trials and clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. We may not be able to initiate or continue to support clinical trials of PINTA 745, EBV-CTL or CMV-CTL or clinical studies for STM 434 or WT1-CTL or any future product candidates if we are unable to locate and enroll a sufficient number of eligible participants in these studies or trials as required by the FDA or other regulatory authorities. Even if we are able to enroll a sufficient number of patients in our clinical studies or trials, if the pace of enrollment is slower than we expect, the development costs for our product candidates may increase and the completion of our studies may be delayed or our studies or trials could become too expensive to

## **Table of Contents**

complete. We rely on CROs, other vendors and clinical study or trial sites to ensure the proper and timely conduct of our clinical studies and trials, and while we have agreements governing their committed activities, we have limited influence over their actual performance.

If we experience delays in the completion or termination of any clinical study or trial of our product candidates, the commercial prospects of such product candidate will be harmed, and our ability to generate product revenues from such product candidate will be delayed. In addition, any delays in completing our clinical studies or trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any delays in completing our clinical studies or trials for the product candidates we have licensed from Amgen or MSK may also decrease the period of commercial exclusivity under our corresponding product candidate license from Amgen or MSK. In addition, many of the factors that could cause a delay in the commencement or completion of clinical studies or trials may also ultimately lead to the denial of regulatory approval of our product candidates.

***Our product candidates, the methods used to deliver them or their dosage levels may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following any regulatory approval.***

Undesirable side effects caused by our product candidates, their delivery methods or dosage levels could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authority. As a result of safety or toxicity issues that we may experience in our clinical studies or trials in the future, we may not receive approval to market any product candidates, which could prevent us from ever generating revenues or achieving profitability. Results of our studies or trials could reveal an unacceptably high severity and prevalence of side effects. In such an event, our studies or trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences may have a material adverse effect on our business, results of operations, financial condition, cash flows and future prospects.

Additionally, if any of our product candidates receives regulatory approval, and we or others later identify undesirable side effects caused by such product, a number of potentially significant negative consequences could result, including that:

we may be forced to suspend marketing of such product;

regulatory authorities may withdraw their approvals of such product;

regulatory authorities may require additional warnings on the label that could diminish the usage or otherwise limit the commercial success of such products;

we may be required to conduct post-market studies;

we may be required to change the way the product is administered;

we could be sued and held liable for harm caused to subjects or patients; and

our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved.



## **Table of Contents**

### ***We may not be able to obtain orphan drug exclusivity for our product candidates.***

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. If our Phase 1 clinical study of STM 434 is successful, we intend to apply for orphan drug status for STM 434 for ovarian cancer. In addition, we may seek orphan drug status for EBV-CTL in rituximab-refractory EBV-LPD after HCT, for EBV-CTL in EBV-LPD after SOT, for CMV-CTL in refractory CMV infection after HCT and for WT1-CTL in AML and multiple myeloma.

Generally, if a product with an orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the European Medicines Agency, or EMA, or the FDA from approving another marketing application for the same drug for that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA 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.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve a new drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

### ***Failure to obtain regulatory approval in international jurisdictions would prevent our product candidates from being marketed abroad.***

In addition to regulations in the United States, to market and sell our products in the European Union, many Asian countries and other jurisdictions, we must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements. We have had no significant interactions with foreign regulatory authorities to date. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. Clinical trials accepted in one country may not be accepted by regulatory authorities in other countries. In addition, many countries outside the United States require that a product be approved for reimbursement before it can be approved for sale in that country. We may not be able to obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market. If we are unable to obtain approval of any of our product candidates by regulatory authorities in the European Union, Asia or elsewhere, the commercial prospects of that product candidate may be significantly diminished, our business prospects could decline and this could materially adversely affect our business, results of operations and financial condition.

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**Table of Contents**

*Even if our product candidates receive regulatory approval, they may still face future development and regulatory difficulties.*

Even if we obtain regulatory approval for a product candidate, it would be subject to ongoing requirements by the FDA and comparable foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, adverse event reporting, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance by our contract manufacturing organizations, or CMOs, and CROs for any post-approval clinical trials that we conduct. For example, if labeling is ultimately approved for PINTA 745, it will likely include restrictions on use due to the specific patient population and manner of use in which the product candidate was evaluated and the safety and efficacy data obtained in those evaluations. In addition, PINTA 745 may be required to include a boxed warning, or black box, regarding PINTA 745 being teratogenic, or causing fetal or embryonic malformations, in animal studies. The safety profile of any product will continue to be closely monitored by the FDA and comparable foreign regulatory authorities after approval. If the FDA or comparable foreign regulatory authorities become aware of new safety information after approval of any of our product candidates, they may require labeling changes or establishment of a risk evaluation and mitigation strategy, impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance.

In addition, 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 current good manufacturing practices, or cGMP, current Good Clinical Practices, or GCP, good tissue practices, or GTPs, and other regulations. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

issue warning letters or untitled letters;

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

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

seek an injunction or impose civil or criminal penalties or monetary fines;

suspend or withdraw regulatory approval;

suspend any ongoing clinical studies;

refuse to approve pending applications or supplements to applications filed 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 require us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate revenues.



## **Table of Contents**

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the Department of Justice, or the DOJ, the Office of Inspector General of the Department of Health and Human Services, or HHS, state attorneys general, members of Congress and the public. Additionally, advertising and promotion of any product candidate that obtains approval outside of the United States will be heavily scrutinized by comparable foreign regulatory authorities. For example, in the event PINTA 745 obtains regulatory approval, we believe these authorities will closely monitor the use of this product candidate to determine whether it is being used impermissibly as a muscle-builder by athletes and others. Violations, including actual or alleged promotion of our products for unapproved or off-label uses, are subject to enforcement letters, inquiries and investigations, and civil and criminal sanctions by the FDA. Any actual or alleged failure to comply with labeling and promotion requirements may have a negative impact on our business.

In the United States, engaging in impermissible promotion of our products for off-label uses can also subject us to false claims litigation under federal and state statutes, which can lead to civil and criminal penalties and fines and agreements that would materially restrict the manner in which we promote or distribute our drug products. These false claims statutes include the federal False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government prevails in the lawsuit, the individual will share in any fines or settlement funds. Since 2004, these False Claims Act lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements based on certain sales practices promoting off-label drug uses. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations, and be excluded from the Medicare, Medicaid and other federal and state healthcare programs. If we do not lawfully promote our approved products, we may become subject to such litigation and, if we are not successful in defending against such actions, those actions could compromise our ability to become profitable or adversely affect our ability to operate our business.

***We are subject to a multitude of manufacturing risks, any of which could substantially increase our costs and limit supply of our product candidates.***

Concurrent with the license of our existing product candidates, we acquired manufacturing process know-how and certain intermediates, as well as certain supplies intended for clinical use, from Amgen and MSK. We are in the process of planning for the manufacture of additional drug substance and drug product for our preclinical and clinical studies using the know-how and supplies we received from Amgen and MSK. Our CMOs will need to conduct significant development work to prepare each of our product candidates for studies, trials and commercial readiness.

The processes by which our product candidates are manufactured were initially developed by Amgen and MSK for clinical purposes. We intend to improve these existing processes for more advanced clinical trials or commercialization. Developing commercially viable manufacturing processes is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including cost overruns, potential problems with process scale-out, process reproducibility, stability issues, lost consistency and timely availability of reagents or raw materials. The manufacturing facilities in which our product candidates will be made could be adversely affected by earthquakes and other natural disasters, equipment failures, labor shortages, power failures, and numerous other factors.



## **Table of Contents**

Additionally, the process of manufacturing biologics and cellular therapies is complex, highly regulated and subject to several risks, including but not limited to:

the process of manufacturing biologics and cellular therapies is extremely susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing processes for any of our product candidates could result in reduced production yields, product defects, and other supply disruptions. Product defects can also occur unexpectedly. For example, in April 2014, we encountered a small number of cracked vials in certain STM 434 drug product lots. If microbial, viral, or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to allow us to investigate and remedy the contamination; and

because EBV-CTL, CMV-CTL and WT1-CTL are manufactured from the blood of third-party donors, the process of developing commercializable products may be particularly challenging, even if they otherwise prove to be safe and effective. The manufacture of these product candidates involves complex processes. Some of these processes require specialized equipment and highly skilled and trained personnel. The process of manufacturing these product candidates will be susceptible to additional risks, given the need to maintain aseptic conditions throughout the manufacturing process. Contamination in the donor material or ingress of microbiological material at any point in the process may result in contaminated and unusable product. Furthermore, the product ultimately consists of many individual cell lines, each with a different HLA profile. As a result, the selection and distribution of the appropriate cell line for therapeutic use in a patient will require close coordination between clinical and manufacturing personnel.

Any adverse developments affecting manufacturing operations for our product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls or other interruptions in the supply of our drug substance and drug product. We may also have to write off inventory, incur other charges and expenses for supply of drug product that fails to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives. Inability to meet the demand for our products could damage our reputation and the reputation of our products among physicians, healthcare payors, patients or the medical community, including major operators of dialysis and cancer clinics, which could adversely affect our ability to operate our business and our results of operations.

***We may not successfully identify, acquire, develop or commercialize new potential product candidates.***

Part of our business strategy is to expand our product candidate pipeline by identifying and validating new product candidates, which we may develop ourselves, in-license or otherwise acquire from others. In addition, in the event that our existing product candidates do not receive regulatory approval or are not successfully commercialized, then the success of our business will depend on our ability to expand our product pipeline through in-licensing or other acquisitions. We may be unable to identify relevant product candidates. If we do identify such product candidates, we may be unable to reach acceptable terms with any third party from which we desire to in-license or acquire them.

***We may not realize the benefits of strategic alliances that we may form in the future.***

We may form strategic alliances, create joint ventures or collaborations or enter into licensing arrangements with third parties that we believe will complement or augment our existing business. These relationships, or those like them, may require us to incur nonrecurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or

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**Table of Contents**

disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic alliances and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic alliance or other alternative arrangements for any future product candidates and programs because our research and development pipeline may be insufficient, our product candidates and programs may be deemed to be at too early a stage of development for collaborative effort and third parties may not view our product candidates and programs as having the requisite potential to demonstrate safety and efficacy. If we license products or acquire businesses, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. We cannot be certain that, following a strategic transaction or license, we will achieve the revenues or specific net income that justifies such transaction. Any delays in entering into new strategic alliances agreements related to our product candidates could also delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

**Risks Related to Our Dependence on Third Parties**

*We rely on third parties to conduct our preclinical and clinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, or if we lose any of our CROs, we may not be able to obtain regulatory approval for or commercialize our product candidates on a timely basis, if at all.*

We have relied upon and plan to continue to rely upon third-party CROs and contractors to monitor and manage data for our ongoing preclinical and clinical programs. For example, our collaborating investigators at MSK manage the conduct of the ongoing clinical studies and trials of EBV-CTL, CMV-CTL and WT1-CTL as well as perform the analysis, publication and presentation of data and results related to these programs. We are also relying on CROs to perform similar services for our ongoing clinical trial of PINTA 745 and clinical study of STM 434. We have also relied on studies previously conducted by Amgen and MSK. We rely on these parties for the execution of our preclinical and clinical trials, and we control only some aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We also rely on third parties to assist in conducting our preclinical studies in accordance with Good Laboratory Practices, or GLP, and the Animal Welfare Act requirements. We and our CROs are required to comply with federal regulations, GCP, which are international standards meant to protect the rights and health of patients that are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for all of our products in clinical development, and GTP, which are standards designed to ensure that cell and tissue based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable diseases. Regulatory authorities enforce GCP and GTP through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP or GTP, 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 regulatory applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP or GTP requirements. In addition, our clinical trials must be conducted with product produced under cGMP requirements. We are also required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, [clinicaltrials.gov](http://clinicaltrials.gov), within a specified timeframe. Failure to comply with these regulations may require us to repeat preclinical and clinical trials, which would delay the regulatory approval process and result in adverse publicity.

## **Table of Contents**

Our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources, including experienced staff, to our ongoing clinical, nonclinical and preclinical programs. They may also have relationships with other entities, some of which may be our competitors. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. For example, there was an error in the randomization of patients and inventory distribution to our clinical sites for our Phase 2 clinical trial for PINTA 745, resulting in the unblinding of the initial six patients and a restart of the trial. CRO or contractor errors could cause our results of operations and the commercial prospects for our product candidates to be harmed, our costs to increase and our ability to generate revenues to be delayed.

Our internal capacity for clinical trial execution and management is limited and therefore we have relied on third parties. Outsourcing these functions involves risk that third parties may not perform to our standards, may not produce results or data in a timely manner or may fail to perform at all. For example, in July 2014, we became aware of a draft report for a preclinical study conducted with STM 217, a compound similar to STM 434 that we also licensed from Amgen. Results from this study led to the amendment of our planned clinical trial for STM 434. Other data from studies previously conducted by Amgen or MSK may emerge in the future. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated. We currently have a small number of employees, which limits the internal resources we have available to identify and monitor our third-party providers. To the extent we are unable to identify and successfully manage the performance of third-party service providers in the future, our business may be adversely affected. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated. Identifying, qualifying and managing performance of third-party service providers can be difficult, time consuming and cause delays in our development programs. In addition, there is a natural transition period when a new CRO commences work and the new CRO may not provide the same type or level of services as the original provider. If any of our relationships with our third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms.

***We have no experience manufacturing our product candidates on a clinical or commercial scale and have no manufacturing facility. We are dependent on third parties for the manufacturing of our product candidates and our supply chain, and if we experience problems with any of these third parties, the manufacturing of our product candidates could be delayed.***

We do not own or operate facilities for the manufacturing of our product candidates. We currently have no commitments to build our own clinical or commercial scale manufacturing capabilities. We currently rely on single source CMOs for the production of the product candidates we have licensed from Amgen and on single source suppliers of some of the materials incorporated in these product candidates. In the case of EBV-CTL, CMV-CTL and WT1-CTL, we rely on MSK for the production of these product candidates and acquisition of the materials incorporated in these product candidates. To

**Table of Contents**

meet our projected needs for clinical supplies to support our activities through regulatory approval and commercial manufacturing of PINTA 745, STM 434 and the other product candidates we have licensed from Amgen, the CMOs with whom we currently work will need to increase the scale of production and demonstrate comparability of the material produced by these CMOs to the material that was previously produced by Amgen. To meet our projected needs for clinical and commercial materials to support our activities through regulatory approval and commercial manufacturing of EBV-CTL, CMV-CTL and WT1-CTL, we will need to transition the manufacturing of such materials to a CMO or our own facility, and such CMOs or we will need to increase the scale of production and demonstrate comparability of the material produced at these facilities to the material that was previously produced by MSK. We need to identify CMOs for the production of EBV-CTL, CMV-CTL and WT1-CTL and may need to identify additional CMOs for continued production of supply for all of our product candidates. In addition, given the manufacturing process for our T-cell product candidates, the number of CMOs who possess the requisite skill and capability to manufacture our T-cell product candidates is limited. We have not yet identified alternate suppliers in the event the current CMOs that we utilize are unable to scale production, or if we otherwise experience any problems with them. Manufacturing biologic drugs is complicated and tightly regulated by the FDA and comparable regulatory authorities around the world, and although alternative third-party suppliers with the necessary manufacturing and regulatory expertise and facilities exist, it could be expensive and take a significant amount of time to arrange for alternative suppliers, transfer manufacturing procedures to these alternative suppliers, and demonstrate comparability of material produced by such new suppliers. New manufacturers of any product would be required to qualify under applicable regulatory requirements. These manufacturers may not be able to manufacture our compounds at costs, or in quantities, or in a timely manner necessary to complete development of our product candidates or make commercially successful products. If we are unable to arrange for alternative third-party manufacturing sources, or to do so on commercially reasonable terms or in a timely manner, we may not be able to complete development of our product candidates, or market or distribute them. In addition, should the FDA not agree with our physical quality specifications and comparability assessments for these materials, further clinical development of our product candidate could be substantially delayed and we would incur substantial additional expenses.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on the third party for regulatory compliance and quality assurance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control, including a failure to synthesize and manufacture our product candidates or any products we may eventually commercialize in accordance with our specifications, misappropriation of our proprietary information, including our trade secrets and know-how, and the possibility of termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or damaging to us. In addition, the FDA and other regulatory authorities require that our product candidates and any products that we may eventually commercialize be manufactured according to cGMP and similar foreign standards. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. The FDA or similar foreign regulatory agencies may also implement new standards at any time, or change their interpretations and enforcement of existing standards for manufacture, packaging or testing of products. We have little control over our manufacturers' compliance with these regulations and standards. Any failure by our third-party manufacturers to comply with cGMP or failure to scale up manufacturing processes, including any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates. In addition, such failure could be the basis for the FDA to issue a warning letter, withdraw approvals for product candidates previously granted to us, or take other regulatory or legal action, including recall or seizure of outside supplies of the product candidate, total or partial suspension of production, suspension of ongoing clinical trials, refusal to approve pending applications or supplemental applications, detention or product, refusal to permit the import or export of products, injunction or imposing civil and criminal penalties.

## **Table of Contents**

Any significant disruption in our supplier relationships could harm our business. Any significant delay in the supply of a product candidate or its key materials for an ongoing clinical study could considerably delay completion of our clinical studies, product testing and potential regulatory approval of our product candidates. If our manufacturers or we are unable to purchase these key materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates could be delayed or there could be a shortage in supply, which could impair our ability to generate revenues from the sale of our product candidates.

### **Risks Related to Our Intellectual Property**

*If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our ability to commercialize our product candidates successfully and to compete effectively may be adversely affected.*

We rely upon a combination of patents, trade secrets and confidentiality agreements to protect the intellectual property related to our technology and product candidates. For our two most advanced molecularly targeted product candidates, PINTA 745 and STM 434, we own or license a number of issued patents and pending patent applications covering the product candidates' compositions of matter and methods of use. For PINTA 745, the expected expiration dates range from 2026 to 2035 for US patents and patent applications, if issued, and from 2023 to 2035 for patents and patent applications, if issued, in jurisdictions outside the United States, exclusive of possible patent term extensions. For STM 434, the expected expiration dates range from 2027 through 2035 for US patents and patent applications, if issued, and from 2026 through 2035 for patents and patent applications, if issued, in jurisdictions outside the United States, exclusive of possible patent term extensions. The T-cell product candidates and platform technology we have licensed from MSK are protected primarily as confidential know-how and trade secrets. If we do not adequately protect our intellectual property, 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. The patentability of inventions and the validity, enforceability and scope of patents in the biotechnology field is generally uncertain because it involves complex legal, scientific and factual considerations, and it has in recent years been the subject of significant litigation. Moreover, the standards applied by the US Patent and Trademark Office, or USPTO, and non-US patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology patents.

Consequently, the patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates in the United States or in other countries for many reasons. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found. We may be unaware of prior art that could be used to invalidate an issued patent or prevent our pending patent applications from issuing as patents. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim of one of our patents or patent applications, which may, nonetheless, ultimately be found to affect the validity or enforceability of such claim.

Even if patents have issued or do successfully issue from patent applications, and even if such patents cover our product candidates, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held to be unenforceable. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. The possibility exists that others will develop products on an independent basis which have the same effect as our product candidates and which do not infringe our

**Table of Contents**

patents or other intellectual property rights, or that others will design around the claims of patents that we have had issued that cover our product candidates. If the breadth or strength of protection provided by the patents and patent applications we hold, license or pursue with respect to our product candidates is threatened, it could threaten our ability to commercialize our product candidates. In addition, the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Any of these outcomes could have an adverse impact on our business.

If patent applications that we hold or in-license with respect to our technology or product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our product candidates, it could dissuade companies from collaborating with us. We have recently filed several patent applications covering our product candidates. We cannot offer any assurances about which, if any, patents will be issued with respect to these pending patent applications, the breadth of any such patents, whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful challenge to these patents or any other patents owned by or exclusively licensed to us could deprive us of rights necessary for the successful commercialization of any product candidate that we or our collaborators may develop. Because patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by the USPTO or a third party to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Similarly, we could become involved in derivation proceedings before the USPTO to determine inventorship with respect to our patent applications. We may also become involved in similar opposition proceedings in the European Patent Office or counterpart offices in other jurisdictions regarding our intellectual property rights. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent generally occurs 20 years after it is filed. Although various extensions may be available if certain conditions are met, the life of a patent and the protection it affords is limited. If we encounter delays in our clinical trials or in obtaining regulatory approvals, the period of time during which we could exclusively market any of our product candidates under patent protection, if approved, could be reduced. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be vulnerable to competition from biosimilar products. Any loss of patent protection could have a material adverse impact on our business. We may be unable to prevent competitors from entering the market with a product that is similar or identical to our product candidates, which could harm our business and ability to achieve profitability.

Furthermore, the research resulting in certain of our licensed patent rights and technology was funded by the US government. As a result, the government may have certain rights, or march-in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to US industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, results of operations, financial condition and future prospects.

## **Table of Contents**

***If we are sued for infringing the intellectual property rights of third parties, such litigation could be costly and time-consuming and could prevent or delay our development and commercialization efforts.***

Our commercial success depends, in part, on us and our collaborators not infringing the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interference or derivation proceedings, oppositions, *inter partes* reexamination and review proceedings before the USPTO and corresponding non-US patent offices. Numerous US and non-US issued patents and pending patent applications owned by third parties exist in the fields in which we are developing and may develop our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of third parties' patent rights as it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform or predictable.

Third parties may assert infringement claims against us based on existing or future intellectual property rights, alleging that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacturing of our product candidates that we failed to identify. For example, applications filed before November 29, 2000, and certain applications filed after that date that will not be filed outside the United States, remain confidential until issued as patents. Except for the preceding exceptions, patent applications in the United States and elsewhere are generally published only after a waiting period of approximately 18 months after the earliest filing date. Therefore, patent applications covering our product candidates could have been filed by others without our knowledge. In addition, pending patent applications that have been published, including some of which we are aware, could be later amended in a manner that could cover our product candidates or their use or manufacture. We may analyze patents or patent applications of our competitors that we believe are relevant to our activities and believe that we are free to operate in relation to any of our product candidates, but our competitors may obtain issued claims, including in patents we consider to be unrelated, which may block our efforts or potentially result in any of our product candidates or our activities infringing such claims. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products and methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving that a patent is invalid is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted, which could have a material adverse effect on us. If any issued third-party patents were held by a court of competent jurisdiction to cover aspects of our materials, formulations, methods of manufacture or methods for treatment, we could be forced, including by court order, to cease developing, manufacturing or commercializing the relevant product candidate until such patent expired. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and to continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms, or at all. Even if we were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property licensed to us. Ultimately, we could be prevented from commercializing a product candidate, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. This could harm our business significantly.

## **Table of Contents**

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent, or to redesign our infringing product candidates which may be impossible or require substantial time and monetary expenditure. We may also elect to enter into license agreements in order to settle patent infringement claims prior to litigation, and any such license agreement may require us to pay royalties and other fees that could be significant.

We may face claims that we misappropriated the confidential information or trade secrets of a third party. If we are found to have misappropriated a third party's trade secrets, we may be prevented from further using such trade secrets, which could limit our ability to develop our product candidates. We are not aware of any material threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. During the course of any patent or other intellectual property litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our product candidates, programs or intellectual property could be diminished. Accordingly, the market price of our common stock may decline.

### ***We may not be able to protect our intellectual property rights throughout the world.***

Filing, prosecuting, enforcing and defending patents on all of our product candidates in all countries throughout the world would be prohibitively expensive. Our or our licensors' intellectual property rights in certain countries outside the United States may be less extensive than those in the United States. In addition, the laws of certain foreign countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we and our licensors may not be able to prevent third parties from practicing our and our licensors' inventions in countries outside the United States, or from selling or importing infringing products made using our and our licensors' inventions in and into the United States or other jurisdictions. Competitors may use our and our licensors' 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 and our licensors have patent protection but where enforcement is not as strong as that in the United States. These infringing products may compete with our product candidates in jurisdictions where we or our licensors have no issued patents and our patent claims and other intellectual property rights may not be effective or sufficient to prevent them from so 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 and our licensors to stop the infringement of our and our licensors' patents or marketing of competing products in violation of our and our licensors' proprietary rights generally. Proceedings to enforce our and our licensors' patent rights in foreign jurisdictions could result in substantial costs and divert our attention from other aspects of our business, could put our and our licensors' patents at risk of being invalidated or interpreted narrowly,



## **Table of Contents**

could put our and our licensors' patent applications at risk of not issuing, and could provoke third parties to assert claims against us or our licensors. We or our licensors may not prevail in any lawsuits that we or our licensors initiate, and even if we or our licensors are successful the damages or other remedies awarded, if any, may not be commercially meaningful.

***We have in-licensed a significant portion of our intellectual property from Amgen and MSK. If we breach any of our license agreements with Amgen or MSK, we could lose the ability to continue the development and potential commercialization of one or more of our product candidates.***

We hold rights under a number of license agreements with Amgen and MSK that are important to our business. Our discovery and development platform is built, in part, around patent rights exclusively in-licensed from Amgen and MSK. The Amgen agreements generally grant us an exclusive (except as to the licenses to Amgen know-how, which are non-exclusive and limited as to their field of use), worldwide (except with regard to PINTA 745 in Japan, which was previously licensed to Takeda Pharmaceutical Company Limited) license to research, develop, improve, make, use, offer for sale, sell, import, export or otherwise exploit several classes of novel compounds, including PINTA 745 and STM 434. The MSK agreement generally grants us an exclusive license to research, develop, make, use, offer for sale, sell and import, EBV-CTL, CMV-CTL and WT1-CTL. Under our existing Amgen and MSK license agreements, we are subject to various obligations, including diligence obligations with respect to development and commercialization activities, payment obligations upon achievement of certain milestones and royalties on product sales, as well as other material obligations. If there is any conflict, dispute, disagreement or issue of nonperformance between us and Amgen or MSK regarding our rights or obligations under the license agreements, including any such conflict, dispute or disagreement arising from our failure to satisfy diligence or payment obligations under any such agreement, we may be liable to pay damages and Amgen or MSK may have a right to terminate the affected license. The loss of any or all of our license agreements with Amgen or our license agreement with MSK could materially adversely affect our ability to proceed to utilize the affected intellectual property in our drug discovery and development efforts, our ability to enter into future collaboration, licensing and/or marketing agreements for one or more affected product candidates and our ability to commercialize the affected product candidates. The risks described elsewhere pertaining to our patents and other intellectual property rights also apply to the intellectual property rights that we license, and any failure by us or our licensors to obtain, maintain and enforce these rights could have a material adverse effect on our business.

***We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful and have a material adverse effect on the success of our business and on our stock price.***

Third parties may infringe our patents, the patents of our licensors, or misappropriate or otherwise violate our or our licensors' intellectual property rights. Our and our licensors' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover the technology. In the future, we or our licensors may elect to initiate legal proceedings to enforce or defend our or our licensors' intellectual property rights, to protect our or our licensors' trade secrets or to determine the validity or scope of intellectual property rights we own or control. Any claims that we assert against perceived infringers could also provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property rights. In addition, third parties may initiate legal proceedings against us or our licensors to challenge the validity or scope of intellectual property rights we own or control. The proceedings can be expensive and time-consuming. Many of our or our licensors' adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensors can. Accordingly, despite our or

## **Table of Contents**

our licensors' efforts, we or our licensors may not be able to prevent third parties from infringing upon or misappropriating intellectual property rights we own or control, particularly in countries where the laws may not protect our rights as fully as in the United States. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, in an infringement proceeding, a court may decide that a patent owned by or licensed to us is invalid or unenforceable, in whole or in part, or may refuse to stop the other party from using the technology at issue on the grounds that our or our licensors' patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our or our licensors' patents at risk of being invalidated, held unenforceable or interpreted narrowly.

Interference or derivation proceedings provoked by third parties, brought by us or our licensors or collaborators, or brought by the USPTO or any non-US patent authority may be necessary to determine the priority of inventions or other matters of inventorship with respect to our patents or patent applications. We may also become involved in other proceedings, such as reexamination or opposition proceedings, *inter partes* review or other preissuance or post-grant proceedings in the USPTO or its foreign counterparts relating to our intellectual property or the intellectual property rights of others. An unfavorable outcome in any such proceeding could require us or our licensors to cease using the related technology and commercializing our product candidates, 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 or our licensors a license on commercially reasonable terms if any license is offered at all. Even if we or our licensors obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensors. In addition, if the breadth or strength of protection provided by our or our licensors' patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Even if we successfully defend such litigation or proceeding, we may incur substantial costs and it may distract our management and other employees. We could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent.

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

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

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity, and obtaining and enforcing biopharmaceutical patents is costly, time-consuming, and inherently uncertain. The 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 and our licensors' ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future decisions by the US Congress, or Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that may weaken our and our licensors' ability to obtain new patents or to enforce existing patents and patents we and our licensors or collaborators may obtain in the future.

## **Table of Contents**

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our and our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to US patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents, all of which could have a material adverse effect on our business and financial condition.

***If we are unable to protect the confidentiality of our trade secrets and other proprietary information, the value of our technology could be materially adversely affected and our business could be harmed.***

In addition to seeking the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce, and other elements of our technology, discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. The T-cell product candidates and platform technology we have licensed from MSK are protected primarily as confidential know-how and trade secrets. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, including by enabling them to develop and commercialize products substantially similar to or competitive with our EBV-CTL, CMV-CTL or WT1 product candidates, thus eroding our competitive position in the market. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements and invention assignment agreements with our employees, consultants, and outside scientific advisors, contractors and collaborators. These agreements are designed to protect our proprietary information. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, or outside scientific advisors might intentionally or inadvertently disclose our trade secrets or confidential, proprietary information to competitors. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. If any of our confidential proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, the laws of certain foreign countries do not protect proprietary rights such as trade secrets to the same extent or in the same manner as the laws of the United States. Misappropriation or unauthorized disclosure of our trade secrets to third parties could impair our competitive advantage in the market and could materially adversely affect our business, results of operations and financial condition.

**Table of Contents**

**Risks Related to Commercialization of Our Product Candidates**

*Our commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, healthcare payors and major operators of dialysis and cancer clinics.*

Even if we obtain regulatory approval for any of our product candidates that we may develop or acquire in the future, the product may not gain market acceptance among physicians, healthcare payors, patients or the medical community, including major operators of dialysis and cancer clinics. Market acceptance of any of our product candidates for which we receive approval depends on a number of factors, including:

the efficacy and safety of such product candidates as demonstrated in clinical trials;

the clinical indications for which the product candidate is approved;

acceptance by physicians, major operators of cancer and dialysis clinics and patients of the drug as a safe and effective treatment;

the adoption of novel cellular therapies by physicians, hospitals and third-party payors;

the potential and perceived advantages of product candidates over alternative treatments;

the safety of product candidates seen in a broader patient group, including its use outside the approved indications;

any restrictions on use together with other medications;

the prevalence and severity of any side effects;

product labeling or product insert requirements of the FDA or other regulatory authorities;

the timing of market introduction of our products as well as competitive products;

the development of manufacturing and distribution processes for our novel T-cell product candidates;

the cost of treatment in relation to alternative treatments;

the availability of coverage and adequate reimbursement and pricing by third-party payors and government authorities;

relative convenience and ease of administration; and

the effectiveness of our sales and marketing efforts and those of our collaborators.

If any of our product candidates are approved but fail to achieve market acceptance among physicians, patients, healthcare payors or major operators of dialysis and cancer clinics, we will not be able to generate significant revenues, which would compromise our ability to become profitable. In particular, the dialysis industry is dominated by two companies, DaVita Healthcare Partners and Fresenius. In the event PINTA 745 fails to be accepted by either of these companies, our ability to generate revenues from PINTA 745 and become profitable could be adversely affected.

***Even if we are able to commercialize our product candidates, the products may not receive coverage and adequate reimbursement from third-party payors in the United States and in other countries in which we seek to commercialize our products, which could harm our business.***

Our ability to commercialize any product successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations.

## **Table of Contents**

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, determine which medications they will cover and establish reimbursement levels. A primary trend in the healthcare industry is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Third-party payors may also seek additional clinical evidence, beyond the data required to obtain regulatory approval, demonstrating clinical benefits and value in specific patient populations before covering our products for those patients. We cannot be sure that coverage and adequate reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain regulatory approval. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate for which we obtain regulatory approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors in the United States often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

***Recently enacted and future legislation, including potentially unfavorable pricing regulations or other healthcare reform initiatives, may increase the difficulty and cost for us to obtain regulatory approval of and commercialize our product candidates and affect the prices we may obtain.***

The regulations that govern, among other things, regulatory approvals, coverage, pricing and reimbursement for new drug products vary widely from country to country. In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay regulatory approval of our product candidates, restrict or regulate post-approval activities and affect our ability to successfully sell any product candidates for which we obtain regulatory approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In particular, all Medicare payments for dialysis treatments to ESRD patients are now made under a single bundled payment rate that provides a fixed payment rate to encompass all goods and services provided during the dialysis treatment, including pharmaceuticals that were

**Table of Contents**

historically separately reimbursed to the dialysis providers, irrespective of the level of pharmaceuticals administered or additional services performed. Most lab services that used to be paid directly to laboratories are also included in the bundled payment. Unless we are able to secure an exemption, PINTA 745 may be subject to the bundled payment system. In recent years, Congress has considered further reductions in Medicare reimbursement for drugs administered by physicians. The Center for Medicare and Medicaid Services, or CMS, the agency that runs the Medicare program, also has the authority to revise reimbursement rates, including under the bundled payment system, and to implement coverage restrictions for some drugs. Cost reduction initiatives and changes in coverage implemented through legislation or regulation could decrease utilization of and reimbursement for any approved products, which in turn would affect the price we can receive for those products. While the Medicare Modernization Act and Medicare regulations apply only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from federal legislation or regulation may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act and the Health Care and Education Affordability Reconciliation Act of 2010, or the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers and impose additional health policy reforms. The Affordable Care Act expanded manufacturers' rebate liability to include covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, increased the minimum rebate due for innovator drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP, and capped the total rebate amount for innovator drugs at 100% of AMP. The Affordable Care Act and subsequent legislation also changed the definition of AMP. Furthermore, the Affordable Care Act imposes a significant annual, nondeductible fee on companies that manufacture or import certain branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may affect our business practices with healthcare practitioners, and a significant number of provisions are not yet, or have only recently become, effective. Although it is too early to determine the effect of the Affordable Care Act, it appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. More recently, in August 2011, the President signed into law the Budget Control Act of 2011, which, among other things, creates the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, 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, starting in 2013. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In March 2013, the President signed an executive order implementing sequestration, and in April 2013, the 2% Medicare reductions went into effect. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and accordingly, our financial operations. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the regulatory approvals of our product candidates, if any, may be.

## **Table of Contents**

In the United States, the European Union and other potentially significant markets for our product candidates, government authorities and third-party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which has resulted in lower average selling prices. Furthermore, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general.

### ***Price controls may be imposed in foreign markets, which may adversely affect our future profitability.***

In some countries, particularly member states of the European Union, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of regulatory approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

### ***We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.***

We face competition from numerous pharmaceutical and biotechnology enterprises, as well as from academic institutions, government agencies and private and public research institutions for our current product candidates. Our commercial opportunities will be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects or are less expensive than any products that we may develop. Competition could result in reduced sales and pricing pressure on our product candidates, if approved, which in turn would reduce our ability to generate meaningful revenues and have a negative impact on our results of operations. In addition, significant delays in the development of our product candidates could allow our competitors to bring products to market before us and impair any ability to commercialize our product candidates.

Products are currently marketed or used off-label for the muscle wasting-related indications for which the products in our pipeline are being developed, and a number of companies are or may be developing new treatments for muscle wasting indications. These products, as well as promotional efforts by competitors and clinical trial results of competitive products, could significantly diminish any ability to market and sell PINTA 745 and other product candidates focused on muscle wasting-related indications. Today's treatment for protein-energy wasting and cancer cachexia often involves the administration of readily available nutritional supplements and appetite stimulants including, in some jurisdictions, medical marijuana. In addition, there are two commercially available steroids, nandrolone and oxandrolone, that are sometimes prescribed off-label for the treatment of weight loss in cancer



## **Table of Contents**

patients. A number of companies are developing drug candidates for muscle wasting applications, including, but not limited to: Eli Lilly & Co., which is conducting Phase 1 clinical studies and Phase 2 clinical trials for LY2495655, and Pfizer Inc., which is conducting Phase 1 clinical studies for PF-06252616, both of which are myostatin antibodies, to evaluate their ability to increase and improve muscle mass in various patient populations; Novartis Corporation, which is conducting Phase 1 clinical studies and Phase 2 clinical trials for BYM338, an ActR2B antibody, to evaluate its ability to build muscle in patients with various muscle-wasting conditions; Ligand Pharmaceuticals, which is developing LGD-4033, a selective androgen receptor modulator, for muscle wasting; Regeneron Pharmaceuticals, Inc., which is developing REGN1033, a myostatin antibody, in collaboration with Sanofi-Aventis for sarcopenia; Acceleron Pharma, Inc., which is developing ACE-083, a modified cysteine knot ligand trap of the TGF- $\beta$  superfamily, for diseases in which improved muscle strength may provide a clinical benefit, such as inclusion body myositis and certain forms of muscular dystrophy; and GTX, Inc., which is developing ostarine, a selective androgen receptor modulator for cachexia.

There are numerous approved products and therapies for ovarian cancer, and a number of companies are or may be developing new treatments for ovarian cancer and other solid tumors. These therapies, as well as promotional efforts by competitors and clinical trial results of competitive products, could significantly diminish any ability to market and sell STM 434. Approved drug therapies for ovarian cancer include: chemotherapy with platinum compounds such as cisplatin or carboplatin and taxane compounds such as paclitaxel or docetaxel; bevacizumab in combination with a chemotherapy compound such as liposomal doxorubicin, paclitaxel or topotecan; olaparib in patients with deleterious or suspected deleterious germline breast cancer susceptibility gene, known as BRCA, mutated advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy; and hormone therapies including goserelin, leuprolide, tamoxifen, letrozole, anastrozole and exemestane. A number of companies are developing drug candidates for ovarian cancer and other solid tumors, including, but not limited to Genentech/Roche, which is developing bevacizumab (Avastin) and other potential drug therapies.

There currently are no FDA or EMA approved products for the treatment of EBV-LPD. However, some approved products and therapies are used off-label in the treatment of EBV-LPD, such as rituximab and combination chemotherapy regimens. In addition, a number of companies and academic institutions are developing drug candidates for EBV-LPD and other EBV associated diseases including: Cell Medica Ltd., or Cell Medica, which is conducting Phase 2 clinical studies for Cytorex EBV, an autologous EBV specific T-cell therapy in NK/T-cell lymphoma; Adcyte LLC, or Adcyte, which has licensed multi-virus specific T-cells from Baylor University that are currently in clinical trials sponsored by Baylor and ViraCyte, which has licensed virus specific T-cells from Baylor University that are currently in clinical trials sponsored by Baylor.

Drug therapies approved or commonly used for CMV infection include antiviral compounds such as ganciclovir, valganciclovir, cidofovir and foscarnet. In addition, a number of companies and academic institutions are developing drug candidates for CMV infection and other CMV-associated diseases, including: Shire Plc, or Shire, which is conducting Phase 2 clinical trials of maribavir, a UL97 protein kinase inhibitor; Merck & Co. Inc., or Merck, which is conducting Phase 3 clinical trials of letermovir, a CMV terminase inhibitor; Chimerix, Inc., or Chimerix, which is conducting Phase 3 clinical trials for brincidofovir, a lipid conjugated nucleotide analogue of cidofovir; Cell Medica, which is conducting Phase 3 clinical trials for Cytovir CMV, a CMV-specific cell therapy product derived from primary HCT transplant donors; Adcyte, which has licensed multi-virus specific T-cells from Baylor University that are currently in clinical trials sponsored by Baylor and ViraCyte, which has licensed virus specific T-cells from Baylor University that are currently in clinical trials sponsored by Baylor.

Many of the approved or commonly used drugs and therapies for muscle wasting, ovarian cancer, EBV-LPD and CMV are well-established and are widely accepted by physicians, patients and third-

## **Table of Contents**

party payors. Some of these drugs are branded and subject to patent protection, and other drugs and nutritional supplements are available on a generic basis. Insurers and other third-party payors may encourage the use of generic products or specific branded products. We expect that, if any of these product candidates is approved, it will be priced at a significant premium over competitive generic products. This pricing premium may make it difficult for us to differentiate these products from currently approved or commonly used therapies and impede adoption of our product, which may adversely impact our business. In addition, many companies are developing new therapeutics, and we cannot predict what the standard of care will become as our products continue in clinical development.

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

As a result of these factors, these competitors may obtain regulatory approval of their products before we are able to obtain patent protection or other intellectual property rights, which will limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are safer, more effective, more widely used and cheaper than ours, and may also be more successful than us in manufacturing and marketing their products. These appreciable advantages could render our product candidates obsolete or noncompetitive before we can recover the expenses of development and commercialization.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

***If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenue.***

We do not currently have an organization for the sale, marketing and distribution of pharmaceutical products and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any products that may be approved by the FDA and comparable foreign regulatory authorities, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. There are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenues and may not become profitable. We will be competing with many companies that currently have extensive and well-funded sales and

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**Table of Contents**

marketing operations. Without an internal commercial organization or the support of a third party to perform sales and marketing functions, we may be unable to compete successfully against these more established companies. If we are not successful in commercializing our current or future product candidates either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we would incur significant additional losses.

*We will need to grow the size of our organization, and we may experience difficulties in managing this growth.*

As of May 31, 2015, we had 29 employees. We need to grow the size of our organization in order to support our continued development and potential commercialization of our product candidates. In particular, we will need to add substantial numbers of additional personnel and other resources to support our development and potential commercialization of EBV-CTL, CMV-CTL and WT1-CTL as a result of our recent exercise of our option to license these programs from MSK. As our development and commercialization plans and strategies continue to develop, or as a result of any future acquisitions, our need for additional managerial, operational, manufacturing, sales, marketing, financial and other resources will increase. Our management, personnel and systems currently in place may not be adequate to support this future growth. Future growth would impose significant added responsibilities on members of management, including:

managing our clinical studies and trials effectively;

identifying, recruiting, maintaining, motivating and integrating additional employees;

managing our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors and other third parties;

improving our managerial, development, operational, information technology, and finance systems; and

expanding our facilities.

As our operations expand, we will also need to manage additional relationships with various strategic partners, suppliers and other third parties. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical studies and trials effectively and hire, train and integrate additional management, research and development, manufacturing, administrative and sales and marketing personnel. Our failure to accomplish any of these tasks could prevent us from successfully growing our company.

***Our future success depends on our ability to retain our executive officers and to attract, retain and motivate qualified personnel.***

We are highly dependent upon our personnel, including Isaac E. Ciechanover, M.D., our President, Chief Executive Officer and founder, and Christopher Haqq, Ph.D., M.D., our Chief Medical Officer. Our employment agreements with Drs. Ciechanover and Haqq are at-will and do not prevent them from terminating their employment with us at any time. The loss of the services of either of them could impede the achievement of our research, development and commercialization objectives.

Our future growth and success depend on our ability to recruit, retain, manage and motivate our employees. The loss of any member of our senior management team or the inability to hire or retain experienced management personnel could compromise our ability to execute our business plan and harm our operating results. Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific, technical and managerial personnel. The competition for qualified personnel in the pharmaceutical field is intense and as a result, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business.

**Table of Contents**

*Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other 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 third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain regulatory approval. Our future arrangements with third-party payors and customers may 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 would market, sell and distribute our products. As a pharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. Restrictions under applicable federal and state healthcare laws and regulations that may affect our ability to operate include the following:

the federal healthcare Anti-Kickback Statute will constrain our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

federal civil and criminal false claims laws and civil monetary penalty laws impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also created federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

the federal physician sunshine requirements under the Affordable Care Act requires manufacturers of drugs, devices, biologics and medical supplies to report annually to HHS information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and

analogous state and foreign laws and regulations, such as state anti-kickback and false claims 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; 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 and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or

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**Table of Contents**

marketing expenditures; and state and foreign laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may 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 are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

***Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.***

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such 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 and results of operations, including the imposition of significant fines or other sanctions.

***Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.***

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling our products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

decreased demand for any product candidates or products that we may develop;

termination of clinical trial sites or entire trial programs;

injury to our reputation and significant negative media attention;

withdrawal of clinical trial participants;

**Table of Contents**

significant costs to defend the related litigation;

substantial monetary awards to trial subjects or patients;

loss of revenue;

diversion of management and scientific resources from our business operations; and

the inability to commercialize any products that we may develop.

We currently hold \$5.0 million in product liability insurance coverage in the aggregate, which we believe is customary for similarly situated companies and adequate to provide us with insurance coverage for foreseeable risks, but which may not be adequate to cover all liabilities that we may incur. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain regulatory approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products that receive regulatory approval. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

***If we and our third-party manufacturers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

We and our third-party manufacturers are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our or our third-party manufacturers' use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.