Celldex Therapeutics, Inc. Form 424B5 February 04, 2013

Use these links to rapidly review the document Table of Contents
TABLE OF CONTENTS

Table of Contents

Filed Pursuant to Rule 424(b)(5) Registration No. 333-185647

The information contained in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any jurisdiction where the offering is not permitted.

SUBJECT TO COMPLETION, DATED FEBRUARY 4, 2013

Prospectus Supplement

(To prospectus dated January 4, 2013)

\$75,000,000

Common Stock

We are offering \$75,000,000 of our common stock. Our common stock is listed on the Nasdaq Global Market under the symbol "CLDX." On February 1, 2013, the last reported sale price of our common stock on the Nasdaq Global Market was \$7.56 per share.

Investing in our common stock involves a high degree of risk. Please read the "Risk Factors" beginning on page S-7 of this prospectus supplement, on page 4 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.

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

	PER SHARE	TOTAL
Public Offering Price	\$	\$
Underwriting Discounts and Commissions	\$	\$
Proceeds to Celldex (Before Expenses)	\$	\$

Delivery of the shares of common stock is expected to be made on or about February , 2013. We have granted the underwriters an option for a period of 30 days to purchase an additional \$11,250,000 of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$ and the total proceeds to us, before expenses, will be \$.

Joint Book-Running Managers

Jefferies

Leerink Swann

Prospectus Supplement dated February , 2013

Table of Contents

Table of Contents

	Page
Prospectus Supplement	
About this Prospectus Supplement	<u>S-1</u>
Our Business	<u>S-2</u>
The Offering	<u>S-2</u> <u>S-6</u>
Risk Factors	<u>S-7</u>
Special Note Regarding Forward-Looking Statements	<u>S-22</u>
<u>Use of Proceeds</u>	<u>S-24</u>
<u>Dilution</u>	<u>S-25</u>
<u>Underwriting</u>	<u>S-26</u>
Notice to Investors	<u>S-30</u>
<u>Legal Matters</u>	<u>S-33</u>
<u>Experts</u>	<u>S-33</u>
Where You Can Find More Information	<u>S-33</u>
<u>Incorporation of Documents by Reference</u>	<u>S-34</u>
Prospectus	
ABOUT THIS PROSPECTUS	<u>1</u>
PROSPECTUS SUMMARY	$\frac{1}{2}$
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	<u>4</u>
RISK FACTORS	<u>4</u>
RATIOS OF COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS TO EARNINGS	4 4 5 5 5 6 7 9
<u>USE OF PROCEEDS</u>	<u>5</u>
<u>DESCRIPTIONS OF SECURITIES WE MAY OFFER</u>	<u>5</u>
DESCRIPTION OF COMMON STOCK	<u>6</u>
DESCRIPTION OF PREFERRED STOCK	<u>7</u>
<u>DESCRIPTION OF WARRANTS</u>	<u>9</u>
<u>DESCRIPTION OF DEPOSITARY SHARES</u>	<u>11</u>
DESCRIPTION OF UNITS	<u>12</u>
<u>PLAN OF DISTRIBUTION</u>	<u>12</u>
<u>LEGAL MATTERS</u>	11 12 12 14 14 14 15
<u>EXPERTS</u>	<u>14</u>
WHERE YOU CAN FIND MORE INFORMATION	<u>14</u>
INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE	<u>15</u>

Table of Contents

About this Prospectus Supplement

In this prospectus supplement, "Celldex," "we," "us," "our" or "ours" refer to Celldex Therapeutics, Inc. and its consolidated subsidiary.

This prospectus supplement and the accompanying prospectus relate to the offering of shares of our common stock. Before buying any of shares of common stock offered hereby, we urge you to carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated herein by reference as described under the headings "Where You Can Find More Information" and "Incorporation of Documents by Reference." These documents contain important information that you should consider when making your investment decision. This prospectus supplement contains information about the common stock offered hereby and may add, update or change information in the accompanying prospectus.

You should rely only on the information that we have provided or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it.

We are not making offers to sell or solicitations to buy our common stock in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information in this prospectus supplement and the accompanying prospectus or any related free writing prospectus is accurate only as of the date on the front of the document and that any information that we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement, the accompanying prospectus or any related free writing prospectus, or any sale of a security.

This document is in two parts. The first part is this prospectus supplement, which adds to and updates information contained in the accompanying prospectus. The second part, the prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus, you should rely on the information in this prospectus supplement.

This prospectus supplement and the accompanying prospectus contain summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been or will be filed as exhibits to the registration statement of which this prospectus is a part or as exhibits to documents incorporated by reference herein, and you may obtain copies of those documents as described below under the headings "Where You Can Find More Information" and "Incorporation of Documents by Reference."

Table of Contents

Our Business

The following summary of our business highlights some of the information contained elsewhere in or incorporated by reference into this prospectus supplement. Because this is only a summary, however, it does not contain all of the information that may be important to you. You should carefully read this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference, which are described under "Incorporation of Documents by Reference" and "Where You Can Find More Information" in this prospectus supplement. You should also carefully consider the matters discussed in the section in this prospectus supplement entitled "Risk Factors" and in the accompanying prospectus and in other periodic reports incorporated by reference herein.

Our Company

We are a biopharmaceutical company focused on the development and commercialization of several immunotherapy technologies for the treatment of cancer and other difficult-to-treat diseases. Our lead drug candidates include rindopepimut (CDX-110), an immunotherapeutic vaccine in a pivotal Phase 3 study for the treatment of front-line glioblastoma and a Phase 2 study for the treatment of recurrent glioblastoma, CDX-011, an antibody-drug conjugate which recently completed a randomized Phase 2b study for the treatment of advanced breast cancer, and CDX-1127, a therapeutic human antibody in a Phase 1 study for cancer indications. We have additional clinical and preclinical programs, including CDX-1401, an APC Targeting Technology program, CDX-301, an immune cell mobilizing agent and dendritic cell growth factor and CDX-1135, a molecule that inhibits a part of the immune system called the complement system. Our drug candidates address market opportunities for which we believe current therapies are inadequate or non-existent.

Generally our strategy is to develop and demonstrate proof-of-concept for our drug candidates before leveraging their value through partnerships or, in appropriate situations, continuing late stage development through commercialization ourselves. Demonstrating proof-of-concept for a drug candidate generally involves bringing it through Phase 1 clinical trials and one or more Phase 2 clinical trials so that we are able to demonstrate, based on human trials, good safety data for the drug candidate and some data indicating its effectiveness. We thus leverage the value of our technology portfolio through corporate, governmental and non-governmental partnerships. This approach allows us to maximize the overall value of our technology and product portfolio while best ensuring the expeditious development of each individual product. Our current collaborations include the commercialization of an oral human rotavirus vaccine. We are exploring potential development and commercialization collaborations for certain drug candidates such as CDX-011 and CDX-1127. Furthermore, while we plan to retain the rights to develop and commercialize rindopepimut in North America, we are exploring potential partnership opportunities to commercialize rindopepimut outside of North America.

Our products are derived from a broad set of complementary technologies which have the ability to utilize the human immune system and enable the creation of therapeutic agents. We are using these technologies to develop targeted immunotherapeutics comprised of antibodies, adjuvants and monotherapies and antibody-drug conjugates that prevent or treat cancer and other diseases that modify undesirable activity by the body's own proteins or cells. A number of our immunotherapeutic and antibody-drug conjugate drug candidates are in various stages of clinical trials. We expect that a large percentage of our research and development expenses will be incurred in support of our current and future clinical trial programs.

Table of Contents

Rindopepimut (CDX-110)

Rindopepimut is an experimental immunothepeutic vaccine that targets the tumor-specific molecule epidermal growth factor receptor variant III, or EGFRvIII. EGFRvIII is a mutated form of the epidermal growth factor receptor, or EGFR, that is only expressed in cancer cells and not in normal tissue and can directly contribute to cancer cell growth. EGFRvIII is expressed in approximately 30% of glioblastoma, or GB, tumors, the most common and aggressive form of brain cancer. The rindopepimut vaccine is composed of the EGFRvIII peptide linked to a carrier protein called Keyhole Limpet Hemocyanin, or KLH, and administered together with the adjuvant GM-CSF. The Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA, have both granted orphan drug designation for rindopepimut for the treatment of EGFRvIII expressing GB. The FDA has also granted Fast Track designation.

Based on the results of the three prior Phase 2 trials, we have entered into a pivotal (registration) program for rindopepimut in patients with surgically resected EGFRvIII-positive GB. In December 2011, we initiated ACT IV, a pivotal, randomized, double-blind, controlled Phase 3 study of rindopepimut, expected to enroll up to 440 patients at over 150 centers worldwide to recruit approximately 374 patients with gross total resection to be included in the primary analysis. Our targeted patient accrual is 24 months and another 18 to 24 months of follow-up. In 2013, we anticipate initiating a parallel, randomized, double-blind, controlled Phase 2 study in western Europe to optimize accrual of the pivotal (registration) study and to further support potential future commercial efforts in this region, assuming rindopepimut is approved by the EMA. We anticipate these two studies to cost over \$60 million during their duration.

Glembatumumab Vedotin (CDX-011)

CDX-011 is an antibody-drug conjugate for the treatment of patients with glycoprotein NMB, referred to as GPNMB, expressing advanced, refractory breast cancer. CDX-011 targets the protein GPNMB, which is over expressed in a variety of cancers, including breast cancer and melanoma. The FDA has granted Fast Track designation to CDX-011 for the treatment of advanced, refractory/resistant GPNMB-expressing breast cancer.

In December 2011, we completed enrollment of EMERGE, a randomized, multi-center Phase 2b study of CDX-011 in 122 patients with heavily pre-treated, advanced, GPNMB positive breast cancer. Patients were randomized (2:1) to receive either CDX-011 or single-agent Investigator's Choice, or IC, chemotherapy. Patients randomized to receive IC are allowed to cross over to receive CDX-011 following disease progression. Activity endpoints include response rate and progression-free survival.

In December 2012, we had our end of Phase 2b meeting with the FDA for our CDX-011 program, which we have characterized as positive. Based on this meeting, we intend to initiate a CDX-011 study suitable for accelerated approval in the second half of 2013. We are currently finalizing the clinical trial design and will update investors on our plans for the accelerated approval trial on our year-end 2012 call in early March 2013.

Also, in December 2012, we announced final results, as shown below, from the EMERGE study which suggested that CDX-011 induces significant response rates compared to currently available therapies in patient subsets with advanced, refractory breast cancers with high GPNMB expression (expression in greater than 25% of tumor cells) and in patients with triple negative breast cancer. The overall survival, or OS, and progression free survival, or PFS, of patients treated with CDX-011 was also observed to be greatest in patients with triple negative breast cancer who also highly express GPNMB and all patients with high GPNMB expression.

Table of Contents

EMERGE: Overall Response Rate and Disease Control Data

On target effect clearly demonstrated in targeted patient populations Triple **Negative** and **Triple High GPNMB High GPNMB All Patients Negative Expression Expression** CDX-011 IC CDX-011 IC CDX-011 IC CDX-011 IC (n=81) (n=36) (n=27) (n=9)(n=25) (n=8) (n=12) (n=4)14% 19% 0% 32% 13% Response 16% 33% 0% Disease Control Rate 57% 53% 67% 33% 64% 38% 75% 25%

Responses per RECIST 1.1; IC = Investigator's Choice; CDX-011 arm includes 15 patients who crossed over to receive CDX-011 treatment after progression on IC. Analysis of best response excludes patients who discontinued from study without evaluable post-baseline radiographic imaging (n=15 for CDX-011 arm; n=5 for IC arm).

EMERGE: Overall Survival (OS) and Progression Free Survival (PFS) Data

On target effect clearly demonstrated in targeted patient populations **Triple Negative** and **Triple High GPNMB High GPNMB All Patients Negative Expression Expression** CDX-011 IC CDX-011 IC CDX-011 IC CDX-011 IC Median OS (months) 7.4 6.5 5.7 p=0.24p=0.18p=0.30p=0.003Median PFS (months) 2.0 2.3 1.5 1.5 2.1 1.6 2.7 3.0 p=0.38p=0.43p=0.14p=0.008

Analyses include all treated patients. Patients who initially received Investigator's Choice (IC) and subsequently crossed over to receive CDX-011 (n=15) are included in the PFS analysis for each treatment. These patients, with a median OS of 12.5 months, are assigned to the IC arm only for OS analysis. Median OS for the remaining IC patients who did not cross over is 5.4 months.

When cross over patients are removed, median OS in patients with high GPNMB expression is 10.0 months for CDX-011 vs 5.2 months for IC (p=0.05) and median OS in triple negative patients with high GPNMB expression is 10.0 months for CDX-011 vs 5.2 months for IC (p=0.009).

CDX-1127

CDX-1127 is a human monoclonal antibody that targets CD27, a potentially important target for immunotherapy of various cancers. CD27 acts downstream from CD40 and may provide a novel way to regulate the immune responses. CD27 is a co-stimulatory molecule on T cells and is

over-expressed in certain lymphomas and leukemias. CDX-1127 is an agonist antibody designed to have two potential therapeutic mechanisms. CDX-1127 has been shown to activate immune cells that can target and eliminate cancerous cells in tumor-bearing mice and to directly kill or inhibit the growth of CD27-expressing lymphomas and leukemias in vitro and in vivo. Both mechanisms have been seen even at low doses in preclinical models.

In November 2011, we initiated an open label, dose-escalating Phase 1 study of CDX-1127 in patients with selected malignant solid tumors or hematologic cancers at multiple clinical sites in the United States. The Phase 1 study is designed to test five escalating doses of CDX-1127 to determine a Phase 2 dose for further development based on safety, tolerability, potential activity and immunogenicity. The study will

Table of Contents

accrue approximately 30 patients in each of the two arms, either selected refractory or relapsed solid tumors or lymphomas or leukemias known to express CD27. Patients will have received all appropriate prior therapies for their specific disease. The trial design incorporates both single dosing and multiple dosing regimens at each dose level. Enrollment has completed in the Phase 1 portion of the solid tumor arm and CDX-1127 was determined to be well tolerated to date, including at the highest dose level. Following a review of the clinical data from these patients, an expansion cohort will be enrolled in 2013. We continue to enroll patients in the dose escalation of the lymphoma and leukemia arm and also plan the initiation of an expansion cohort of this arm in 2013. We anticipate data from the CDX-1127 program in the second half of 2013.

Other Clinical and Pre-Clinical Programs

We have several other programs in clinical and pre-clinical development. The status of the other programs that we currently believe are material to our business is summarized in the table below:

Product Candidate	Indication/Field	Stage of Clinical Development
CDX-1401	Multiple solid tumors	Phase 1
	Cancer, autoimmune disease and	
CDX-301	transplant	Phase 1
CDX-1135	Renal disease	Pilot

Rotarix

In 1997, we licensed our oral rotavirus strain to GlaxoSmithKline plc, or Glaxo, and Glaxo assumed responsibility for all subsequent clinical trials and all other development activities. We licensed-in the rotavirus strain that was used to develop Glaxo's Rotarix rotavirus vaccine in 1995 and owe a license fee of 30% to Cincinnati Children's Hospital Medical Center, or CCH, on net royalties received from Glaxo. In May 2005, we entered into an agreement whereby an affiliate of Paul Royalty Fund II, L.P., or PRF, purchased a 70% interest in the net royalties we receive on worldwide sales of Rotarix under the Glaxo agreement.

In December 2012, a U.S. patent for our rotavirus strain that we licensed to Glaxo expired. The Glaxo agreement terminates automatically upon the expiration, lapse or invalidation of the last relevant patent right (patent or patent application) covered by the Glaxo agreement, although Glaxo may terminate the agreement upon 90 days prior written notice. The only remaining relevant patent right is a patent application in Mexico with a projected final expiry date in May 2013 which is under appeal. The PRF agreement provided for a normal expiry of the PRF agreement on December 12, 2012 except that the PRF agreement stays in effect until PRF receives their final royalty payment which is expected to be received in the first quarter of 2013. In addition, the PRF agreement provides for an exclusive 120-day right of negotiation for extension in certain circumstances.

Corporate Information

We are a Delaware corporation organized in 1983. On October 1, 2009, a wholly-owned subsidiary of Celldex merged with and into CuraGen Corporation. On December 31, 2009, CuraGen Corporation was merged with and into Celldex and the separate existence of CuraGen ceased.

Our principal executive offices are located at 119 Fourth Avenue, Needham, Massachusetts 02494 and our telephone number is (781) 433-0771. Our corporate website is www.celldextherapeutics.com. The information on our website is not incorporated by reference into this prospectus.

Table of Contents

The Offering

Common stock offered by us shares

Common stock to be outstanding immediately

after this offering shares

Underwriters' Option to Purchase Additional Shares

We have granted the underwriters an option to purchase up to additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.

Use of Proceeds

We intend to use the net proceeds to fund clinical trials of our product candidates and for working capital and other general corporate purposes. See "Use of Proceeds."

Risk Factors

An investment in our common stock involves a high degree of risk. See the information contained in or incorporated under "Risk Factors" beginning on page S-7 of this prospectus supplement, page 4 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.

Nasdaq Global Market Symbol

Our common stock is listed on The Nasdaq Global Market under the symbol "CLDX."

The total number of shares of common stock to be outstanding immediately after this offering assumes no exercise of the underwriters' option to purchase additional shares and is based on 66,795,069 shares of common stock issued and outstanding as of February 1, 2013, which does not include the following, all as of September 30, 2012:

5,351,999 shares issuable upon the exercise of outstanding stock options with a weighted-average exercise price of \$5.97 per share; and

3,380,865 shares available for future issuance under our equity compensation plans.

Unless otherwise stated, all information in this prospectus supplement:

assumes no exercise of outstanding options to purchase common stock, no issuance of shares available for future issuance under our equity compensation plans, and no conversion of our convertible notes;

assumes no exercise of the underwriters' option to purchase additional shares; and

reflects all currency in U.S. dollars.

Table of Contents

Risk Factors

An investment in our securities involves a high degree of risk. You should carefully consider the risks described under "Risk Factors" in the accompanying prospectus, our Annual Report on Form 10-K for the year ended December 31, 2011 and our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2012, June 30, 2012 and September 30, 2012, respectively, as updated by any other document that we subsequently file with the Securities and Exchange Commission and that is incorporated by reference into this prospectus supplement and the accompanying prospectus, as well as the risks described below and all of the other information contained in this prospectus supplement and the accompanying prospectus, and incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements and related notes, before investing in our securities. If any of the possible events described in those sections or below actually occur, our business, business prospects, cash flow, results of operations or financial condition could be harmed. In such case, the trading price of our common stock could decline, and you could lose all or part of your investment in our common stock.

The following is a discussion of the risk factors that we believe are material to us at this time. These risks and uncertainties are not the only ones facing us and there may be additional matters that we are unaware of or that we currently consider immaterial. All of these could adversely affect our business, business prospects, cash flow, results of operations and financial condition.

Risks Related to our Business

We currently have no product revenue and will need to raise capital to operate our business in addition to funds we receive in this offering.

To date, we have generated no product revenue and cannot predict when and if we will generate product revenue. We had an accumulated deficit of \$247 million as of September 30, 2012. Until, and unless, we complete clinical trials and further development, and receive approval from the FDA and other regulatory authorities, for our product candidates, we cannot sell our drugs and will not have product revenue. We expect to spend substantial funds to continue the research and development testing of our products that are in the preclinical and clinical testing stages of development and to prepare to commercialize products in anticipation of FDA approval. Therefore, for the foreseeable future, we will have to fund all of our operations and development expenditures from cash on hand, equity or debt financings, licensing fees and grants. While the funds we receive in this offering will help fund our operations, additional financing will also be required. If we do not succeed in raising additional funds on acceptable terms, we might not be able to complete planned preclinical and clinical trials or obtain approval of any product candidates from the FDA and other regulatory authorities. In addition, we could be forced to discontinue product development, reduce or forego sales and marketing efforts, forego attractive business opportunities or curtail operations. Any additional sources of financing could involve the issuance of our equity securities, which would have a dilutive effect on our stockholders. No assurance can be given that additional financing will be available to us when needed on acceptable terms, or at all.

We cannot be certain that we will achieve or sustain profitability in the future. Failure to achieve profitability could diminish our ability to sustain operations, pay dividends on our common stock, obtain additional required funds and make required payments on our present or future indebtedness.

We expect to incur future losses and we may never become profitable.

We have incurred operating losses of \$41.5 million in the nine months ended September 30, 2012, and of \$43.4 million, \$6.5 million and \$36.9 million during 2011, 2010 and 2009, respectively, and expect to incur an operating loss in the fourth quarter of 2012 and in 2013. We believe that operating losses will continue in and beyond 2013 because we are planning to incur significant costs associated with the clinical development and manufacturing commercial supply of rindopepimut to prepare for the potential launch of

Table of Contents

rindopepimut. In addition, we are planning to incur significant costs in the clinical development of CDX-011, CDX-1127, CDX-1401, CDX-301 and CDX-1135. Our net losses have had and will continue to have an adverse effect on, among other things, our stockholders' equity, total assets and working capital. We expect that losses will fluctuate from quarter to quarter and year to year, and that such fluctuations may be substantial. We cannot predict when we will become profitable, if at all.

Our long term success depends heavily on our ability to fund and complete research and development activities for, and to commercialize, our lead drug candidate, rindopepimut, which we are developing internally.

While in the past we have typically focused on developing and demonstrating proof-of-concept for our product candidates by bringing such candidates through Phase 1 and one or more Phase 2 clinical trials, and then leveraging their value through partnerships, we have decided to fund and complete the research and development activities for rindopepimut ourselves. We plan to commercialize rindopepimut ourselves in North America and to find a partner to commercialize rindopepimut outside of North America. Therefore, we must allocate a significant portion of our time, personnel and financial resources to the development of rindopepimut. We initiated ACT IV, our pivotal Phase 3 clinical trial of rindopepimut, in December 2011. While we are targeting two years for patient accrual, it could take up to three years to enroll all the patients, and another 18 to 24 months of follow-up. We plan to initiate a parallel Phase 2 study in western Europe. We anticipate these two studies to cost over \$60 million during their duration. Our management team lacks significant experience in completing Phase 3 clinical trials and bringing a drug through commercialization. If we face delays, difficulties or unanticipated costs in completing the development of rindopepimut, we will need substantial additional financing. Further, even if we complete the development of rindopepimut and gain marketing approvals from the FDA and comparable foreign regulatory authorities in a timely manner, we cannot be sure that rindopepimut will be commercially successful in the pharmaceutical market. If the results of clinical trials of rindopepimut, the anticipated or actual timing of marketing approvals for rindopepimut, or the market acceptance of rindopepimut, if approved, do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline.

We will need additional capital to fund our operations, including the development, manufacture and potential commercialization of our drug candidates. If we do not have or cannot raise additional capital when needed, we will be unable to develop and ultimately commercialize our drug candidates successfully.

We expect to incur significant costs as we develop our drug candidates. In particular, the continuing development and commercialization of rindopepimut requires additional capital beyond our current resources. As of September 30, 2012, we had cash, cash equivalents and marketable securities of \$77.6 million.

We may take further steps to raise additional capital to fund our long-term liquidity needs. Our capital raising activities may include, but may not be limited to, one or more of the following:

licensing of drug candidates with existing or new collaborative partners;
possible business combinations;
issuance of debt; or
issuance of common stock or other securities via private placements or public offerings.

While we may continue to seek capital through a number of means, there can be no assurance that additional financing will be available on acceptable terms, if at all, and our negotiating position in capital-raising efforts may worsen as existing resources are used. There is also no assurance that we will be able to enter into further collaborative relationships. Additional equity financing may be dilutive to our stockholders; debt financing, if available, may involve significant cash payment obligations and covenants that restrict our ability to operate as a business; and licensing or strategic collaborations may result in royalties or other terms which reduce our economic potential from products under development. If we are unable to raise the

Table of Contents

funds necessary to meet our long-term liquidity needs, we may have to delay or discontinue the development of one or more programs, discontinue or delay on-going or anticipated clinical trials, license out programs earlier than expected, raise funds at significant discount or on other unfavorable terms, if at all, or sell all or part of our business.

Since September 30, 2012, we have issued 5,954,798 shares of our common stock for aggregate net proceeds of approximately \$38.0 million pursuant to our equity line agreement with Cantor Fitzgerald & Co., or the Cantor Agreement. The Cantor Agreement provides for the sale of an amount of shares of our common stock having an aggregate offering price of up to \$44,000,000 from time to time into the open market at prevailing prices. As of February 1, 2013, shares of common stock having an aggregate offering price of up to \$4.4 million remain available for issuance under the equity line. Under the terms of our lock up agreement with the underwriters of this offering, we may resume selling our common stock under the equity line as early as 90 days after this offering is consummated. See "Underwriting."

We may be unable to manage one Phase 3 clinical trial or multiple late stage clinical trials for a variety of product candidates simultaneously.

As our current clinical trials progress, we may need to manage multiple late stage clinical trials simultaneously in order to continue developing all of our current products. Our management team does not have significant experience in completing late stage clinical trials and the management of late stage clinical trials is more complex and time consuming than early stage trials. Typically, early stage trials involve several hundred patients in no more than 10-30 clinical sites. Late stage (Phase 3) trials may involve up to several thousand patients in up to several hundred clinical sites and may require facilities in several countries. Therefore, the project management required to supervise and control such an extensive program is substantially larger than early stage programs. As the need for these resources is not known until some months before the trials begin, it is necessary to recruit large numbers of experienced and talented individuals very quickly. If the labor market does not allow this team to be recruited quickly, the sponsor is faced with a decision to delay the program or to initiate it with inadequate management resources. This may result in recruitment of inappropriate patients, inadequate monitoring of clinical investigators and inappropriate handling of data or data analysis. Consequently it is possible that conclusions of efficacy or safety may not be acceptable to permit filing of a BLA or NDA for any one of the above reasons or a combination of several.

We rely on third parties to plan, conduct and monitor our clinical tests, and their failure to perform as required would interfere with our product development.

We rely on third parties to conduct a significant portion of our clinical development activities. These activities include clinical patient recruitment and observation, clinical trial monitoring, clinical data management and analysis, safety monitoring and project management. We conduct project management and medical and safety monitoring in-house for some of our programs and rely on third parties for the remainder of our clinical development activities.

The significant third parties who we currently rely on for clinical development activities include Novella Clinical Inc. for our ACT IV study. If Novella is unable to perform in a quality and timely manner, and at a feasible cost, ACT IV will face delays. Further, if any of these third parties fails to perform as we expect or if their work fails to meet regulatory standards, our testing could be delayed, cancelled or rendered ineffective.

Table of Contents

We may enter into collaboration agreements for the licensing, development and ultimate commercialization of some of our drug candidates including, where appropriate, for our lead drug candidates. In such cases, we will depend greatly on our third party collaborators to license, develop and commercialize such drug candidates, and they may not meet our expectations.

We are exploring potential co-development and commercialization partnerships for certain products, including rindopepimut for commercialization outside of North America, CDX-011 and CDX-1127. The process of identifying collaborators and negotiating collaboration agreements for the licensing, development and ultimate commercialization of some of our drug candidates may cause delays and increased costs. We may not be able to enter into collaboration agreements on terms favorable to us. Furthermore some of those agreements may give substantial responsibility over our drug candidates to the collaborator. Some collaborators may be unable or unwilling to devote sufficient resources to develop our drug candidates as their agreements require. They often face business risks similar to ours, and this could interfere with their efforts. Also, collaborators may choose to devote their resources to products that compete with ours. If a collaborator does not successfully develop any one of our products, we will need to find another collaborator to do so. The success of our search for a new collaborator will depend on our legal right to do so at the time and whether the product remains commercially viable.

If we enter into collaboration agreements for one or more of our lead drug candidates, the success of such drug candidates will depend in great part upon our and our collaborators' success in promoting them as superior to other treatment alternatives. We believe that our drug candidates can be proven to offer disease prevention and treatment with notable advantages over drugs in terms of patient compliance and effectiveness. However, there can be no assurance that we will be able to prove these advantages or that the advantages will be sufficient to support the successful commercialization of our drug candidates.

We may face delays, difficulties or unanticipated costs in establishing sales, distribution and manufacturing capabilities for our commercially ready products.

Our current plan is to retain, rather than license to a third party, all rights to rindopepimut in North America (and to explore partnership opportunities to commercialize rindopepimut outside of North America) and our APC Targeting Technology programs. As a result, we will have full responsibility for commercialization of these products if and when they are approved for sale. We currently lack the marketing, sales and distribution capabilities that we will need to carry out this strategy. To market any of our products directly, we must develop a substantial marketing and sales force with technical expertise and a supporting distribution capability. We have little expertise in this area, and we may not succeed. We may find it necessary to enter into strategic partnerships on uncertain but potentially unfavorable terms to sell, market and distribute our products when they are approved for sale.

Some of our products are difficult to manufacture, especially in large quantities, and we have not yet developed commercial scale manufacturing processes for any of our products. We do not currently plan to develop internal manufacturing capabilities to produce any of our products at commercial scale if they are approved for sale. To the extent that we choose to market and distribute these products ourselves, this strategy will make us dependent on other companies to produce our products in adequate quantities, in compliance with regulatory requirements, and at a competitive cost. We may not find third parties capable of meeting those manufacturing needs.

Our drug candidates are subject to extensive regulatory scrutiny.

All of our drug candidates are at various stages of development and commercialization and our activities and drug candidates are significantly regulated by a number of governmental entities, including the FDA in the United States and by comparable authorities in other countries. These entities regulate, among other things, the manufacture, testing, safety, effectiveness, labeling, documentation, advertising and sale of drugs and drug candidates. We or our partners must obtain regulatory approval for a drug candidate in all of

Table of Contents

these areas before we can commercialize the drug candidate. Product development within this regulatory framework takes a number of years and involves the expenditure of substantial resources. This process typically requires extensive preclinical and clinical testing, which may take longer or cost more than we anticipate, and may prove unsuccessful due to numerous factors. Many drug candidates that initially appear promising ultimately do not reach the market because they are found to be unsafe or ineffective when tested. Companies in the pharmaceutical, biotechnology and vaccines industries have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier trials. Our inability to commercialize a drug candidate would impair our ability to earn future revenues.

If our products do not pass required tests for safety and effectiveness, we will not be able to derive commercial revenue from them.

In order to succeed, we will need to derive commercial revenue from the products we have under development. The FDA has not approved our rindopepimut, CDX-011 or CDX-1127 drug candidates or any of our other products for sale to date. Our drug candidates are in various stages of preclinical and clinical testing. Preclinical tests are performed at an early stage of a product's development and provide information about a product's safety and effectiveness on laboratory animals. Preclinical tests can last years. If a product passes its preclinical tests satisfactorily, and we determine that further development is warranted, we would file an IND application for the product with the FDA, and if the FDA gives its approval we would begin Phase 1 clinical tests. Phase 1 testing generally lasts between 6 and 24 months. If Phase 1 test results are satisfactory and the FDA gives its approval, we can begin Phase 2 clinical tests. Phase 2 testing generally lasts between 6 and 36 months. If Phase 2 test results are satisfactory and the FDA gives its approval, we can begin Phase 3 pivotal studies. Phase 3 studies generally last between 12 and 48 months. Once clinical testing is completed and a new drug application is filed with the FDA, it may take more than a year to receive FDA approval.

In all cases we must show that a pharmaceutical product is both safe and effective before the FDA, or drug approval agencies of other countries where we intend to sell the product, will approve it for sale. Our research and testing programs must comply with drug approval requirements both in the United States and in other countries, since we are developing our lead products with the intention to, or could later decide to, commercialize them both in the U.S. and abroad. A product may fail for safety or effectiveness at any stage of the testing process. A major risk we face is the possibility that none of our products under development will come through the testing process to final approval for sale, with the result that we cannot derive any commercial revenue from them after investing significant amounts of capital in multiple stages of preclinical and clinical testing.

Product testing is critical to the success of our products but subject to delay or cancellation if we have difficulty enrolling patients.

As our portfolio of potential products moves from preclinical testing to clinical testing, and then through progressively larger and more complex clinical trials, we will need to enroll an increasing number of patients with the appropriate characteristics. At times we have experienced difficulty enrolling patients and we may experience more difficulty as the scale of our clinical testing program increases. The factors that affect our ability to enroll patients are largely uncontrollable and include principally the following:

the nature of the clinical test;
the size of the patient population;
patients' willingness to receive a placebo or less effective treatment on the control arm of a clinical study;
the distance between patients and clinical test sites; and
the eligibility criteria for the trial.
S 11

Table of Contents

If we cannot enroll patients as needed, our costs may increase or it could force us to delay or terminate testing for a product.

We may have delays in completing our clinical trials and we may not complete them at all.

We have not completed the clinical trials necessary to obtain FDA approval to market rindopepimut, CDX-011 or any of our other products in development. We initiated a Phase 3 study of rindopepimut in December 2011 but we have not initiated Phase 3 studies for CDX-011 or any of our other products in development. Our management lacks significant experience in completing Phase 3 trials and bringing a drug through commercialization. Our rindopepimut Phase 3 trial, CDX-011 late-stage studies and planned clinical trials for other products in development may be delayed or terminated as a result of many factors, including the following:

difficulty in enrolling patients in our clinical trials;

patients failing to complete clinical trials due to dissatisfaction with the treatment, side effects or other reasons;

failure by regulators to authorize us to commence a clinical trial;

suspension or termination by regulators of clinical research for many reasons, including concerns about patient safety or failure of our contract manufacturers to comply with cGMP requirements;

delays or failure of the FDA to remove the clinical hold on our CDX-011 studies;

treatment candidates demonstrating a lack of efficacy during clinical trials;

inability to continue to fund clinical trials or to find a partner to fund the clinical trials;

competition with ongoing clinical trials and scheduling conflicts with participating clinicians; and

delays in completing data collection and analysis for clinical trials.

Any delay or failure to complete clinical trials and obtain FDA approval for our drug candidates could have a material adverse effect on our cost to develop and commercialize, and our ability to generate revenue from, a particular drug candidate.

Any delay in obtaining regulatory approval would have an adverse impact on our ability to earn future revenues.

It is possible that none of the drug candidates that we develop will obtain the regulatory approvals necessary for us to begin commercializing them. The time required to obtain FDA and other approvals is unpredictable but often can take years following the commencement of clinical trials, depending upon the nature of the drug candidate. Any analysis we perform of data from clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular drug candidate including, but not limited to, loss of patent term during the approval period. Furthermore, if we, or our partners, do not reach the market with our products before our competitors offer products for the same or similar uses, or if we, or our partners, are not effective in marketing our products, our revenues from product sales, if any, will be reduced.

We face intense competition in our development activities. We face competition from many companies in the United States and abroad, including a number of large pharmaceutical companies, firms specialized in the development and production of vaccines, adjuvants and vaccine and immunotherapeutic delivery systems and major universities and research institutions. The competitors for which we are aware have initiated

a Phase 3 study or have obtained marketing approval for a potentially competitive drug include Alexion, Agenus, Baxter, BMS, Dendreon, Eli Lilly, GlaxoSmithKline, ImmunoGen, Merck, Pfizer, Roche, Sanofi-Aventis, Seattle Genetics, and Takeda. Most of our competitors have substantially greater resources, more extensive experience in conducting preclinical studies and clinical testing and obtaining regulatory approvals for their products, greater operating experience, greater research and development and marketing

Table of Contents

capabilities and greater production capabilities than those of ours. These companies might succeed in obtaining regulatory approval for competitive products more rapidly than we can for our products, especially if we experience any delay in obtaining required regulatory approvals.

Failure to comply with applicable regulatory requirements would adversely impact our operations.

Even after receiving regulatory approval, our products would be subject to extensive regulatory requirements, and our failure to comply with applicable regulatory requirements will adversely impact our operations. In the United States, the FDA requires that the manufacturing facility that produces a product meet specified standards, undergo an inspection and obtain an establishment license prior to commercial marketing. Subsequent discovery of previously unknown problems with a product or its manufacturing process may result in restrictions on the product or the manufacturer, including withdrawal of the product from the market. Failure to comply with the applicable regulatory requirements can result in fines, suspensions of regulatory approvals, product recalls, operating restrictions and criminal prosecution.

We depend greatly on the intellectual capabilities and experience of our key executives and scientists and the loss of any of them could affect our ability to develop our products.

The loss of Anthony S. Marucci, our President and Chief Executive Officer, or other key members of our staff, including Avery W. Catlin, our Chief Financial Officer, Dr. Thomas Davis, our Chief Medical Officer, Dr. Tibor Keler, our Chief Scientific Officer or Dr. Ronald Pepin, our Chief Business Officer, could harm us. We entered into employment agreements with Messrs. Marucci, Catlin, Davis, Keler and Pepin although an employment agreement as a practical matter does not guarantee retention of an employee. We also depend on our scientific and clinical collaborators and advisors, all of whom have outside commitments that may limit their availability to us. In addition, we believe that our future success will depend in large part upon our ability to attract and retain highly skilled scientific, managerial and marketing personnel, particularly as we expand our activities in clinical trials, the regulatory approval process and sales and manufacturing. We routinely enter into consulting agreements with our scientific and clinical collaborators and advisors, key opinion leaders and heads of academic departments in the ordinary course of our business. We also enter into contractual agreements with physicians and institutions who recruit patients into our clinical trials on our behalf in the ordinary course of our business. Notwithstanding these arrangements, we face significant competition for this type of personnel from other companies, research and academic institutions, government entities and other organizations. We cannot predict our success in hiring or retaining the personnel we require for continued growth.

We rely on contract manufacturers over whom we have limited control. Should the cost, delivery and quality of clinical and commercial grade materials supplied by contract manufacturers vary to our disadvantage, our business operations could suffer significant harm.

We have limited experience in large scale manufacturing at our Fall River facility. We have manufactured clinical materials of CDX-1127, CDX-1135, CDX-1401 and CDX-301 in our Fall River facility for our current and planned Phase 1 and Phase 2 clinical trials. We rely on sourcing from third-party manufacturers for suitable quantities of our late-stage clinical and commercial grade materials and certain filling and packaging essential to preclinical and clinical studies currently underway and for planned clinical trials in addition to those currently being conducted by third parties or us.

In 2013, we plan to establish a relationship with a contract manufacturer to produce the required commercial manufacturing lots of rindopepimut necessary for commercial launch. The inability to have suitable quality and quantities of these essential materials produced in a timely manner would result in significant delays in the clinical development and commercialization of products, which could adversely affect our business, financial condition and results of operations.

Table of Contents

One lot of our CDX-011 product candidate used in our Phase 2b study was aseptically filled in 2009 by Formatech, a third party contract manufacturer. The CDX-011 lot from Formatech passed all of the sterility testing performed during drug release and in subsequent stability studies. At the end of January 2012, we were notified by the FDA that because significant Good Manufacturing Practice, or cGMP, violations were uncovered during inspection of Formatech, our Phase 2b study for CDX-011 was being placed on partial clinical hold. The FDA uncovered these findings during their inspections of the Formatech facility between August to October 2010 and July to August 2011. These inspections began approximately one year after the CDX-011 drug product was filled at Formatech. Specifically, the FDA requested that no new patients be treated with CDX-011. However, patients already undergoing treatment with CDX-011 were allowed to continue treatment using vials of CDX-011 from the lot filled by Formatech, after such patients were informed of the potential risk and reconsented to continued participation in the study. The FDA also agreed that patients in IC arm of the study who became eligible to receive CDX-011 at the time of progression, could receive an older lot of CDX-011 until such time that the material was exhausted or expired. As such, this clinical hold did not significantly impact the conduct or analysis of the Phase 2b study for purposes of determining next steps in our future development of CDX-011. With respect to future clinical trials, the FDA has converted the partial clinical hold to a clinical hold pending successful completion of reprocessing of the CDX-011 manufactured at Formatech or submission of an alternate cGMP manufacturing site for future lots of CDX-011. The FDA has agreed in concept that we could reprocess the remaining available vials of CDX-011 manufactured at Formatech at another cGMP contract manufacturer in order to lift the clinical hold. The FDA's final decision regarding the acceptability of this reprocessing will be made upon review of data concerning the stability and sterility of the reprocessed vials of CDX-011. If we are unsuccessful at reprocessing the available drug product or if FDA does not approve the use of these reprocessed vials, we will need to manufacture new drug product for subsequent clinical studies for CDX-011. We have initiated the manufacturing of the next lot of CDX-011 and we expect that it will be available for the initiation of our late-stage trial with CDX-011.

We also rely on collaborators and contract manufacturers to manufacture proposed products in both clinical and commercial quantities in the future. Our leading vaccine candidates require specialized manufacturing capabilities and processes. We may face difficulty in securing commitments from U.S. and foreign contract manufacturers as these manufacturers could be unwilling or unable to accommodate our needs. Relying on foreign manufacturers involves peculiar and increased risks, including the risk relating to the difficulty foreign manufacturers may face in complying with GMP requirements as a result of language barriers, lack of familiarity with GMP or the FDA regulatory process or other causes, economic or political instability in or affecting the home countries of our foreign manufacturers, shipping delays, potential changes in foreign regulatory laws governing the sales of our product supplies, fluctuations in foreign currency exchange rates and the imposition or application of trade restrictions.

There can be no assurances that we will be able to enter into long-term arrangements with third party manufacturers on acceptable terms, or at all. Further, contract manufacturers must also be able to meet our timetable and requirements, and must operate in compliance with GMP; failure to do so could result in, among other things, the disruption of product supplies. As noted above, non-U.S. contract manufacturers may face special challenges in complying with GMP requirements, and although we are not currently dependent on non-U.S. collaborators or contract manufacturers, we may choose or be required to rely on non-U.S. sources in the future as we seek to develop stable supplies of increasing quantities of materials for ongoing clinical trials of larger scale. Our dependence upon third parties for the manufacture of our products may adversely affect our profit margins and our ability to develop and deliver products on a timely and competitive basis.

The significant third parties who we currently rely on for sourcing of suitable quantities of some of our clinical and commercial grade materials include Biosyn, Bayer and Sanofi for our rindopepimut drug candidate. If we or our third-party manufacturers are unable to produce drug material in suitable quantities of appropriate quality, in a timely manner, and at a feasible cost, our clinical tests will face delays.

Table of Contents

Other factors could affect the demand for and sales of any products that we may commercialize in the future.

In general, other factors that could affect the demand for and sales and profitability of our products include, but are not limited to:

the timing of regulatory approval, if any, of competitive products;

our or any other of our partners' pricing decisions, as applicable, including a decision to increase or decrease the price of a product, and the pricing decisions of our competitors;

government and third-party payer reimbursement and coverage decisions that affect the utilization of our products and competing products;

negative safety or efficacy data from new clinical studies conducted either in the U.S. or internationally by any party could cause the sales of our products to decrease or a product to be recalled;

the degree of patent protection afforded our products by patents granted to or licensed by us and by the outcome of litigation involving our or any of our licensor's patents;

the outcome of litigation involving patents of other companies concerning our products or processes related to production and formulation of those products or uses of those products;

the increasing use and development of alternate therapies;

the rate of market penetration by competing products; and

the termination of, or change in, existing arrangements with our partners.

Any of these factors could have a material adverse effect on the sales of any products that we may commercialize in the future.

We face the risk of product liability claims, which could exceed our insurance coverage, and produce recalls, each of which could deplete our cash resources.

As a participant in the pharmaceutical, biotechnology and vaccines industries, we are exposed to the risk of product liability claims alleging that use of our drug candidates caused an injury or harm. These claims can arise at any point in the development, testing, manufacture, marketing or sale of our drug candidates and may be made directly by patients involved in clinical trials of our products, by consumers or healthcare providers or by individuals, organizations or companies selling our products. Product liability claims can be expensive to defend, even if the drug or drug candidate did not actually cause the alleged injury or harm.

Insurance covering product liability claims becomes increasingly expensive as a drug candidate moves through the development pipeline to commercialization. Under our license agreements, we are required to maintain clinical trial liability insurance coverage up to \$14 million. However, there can be no assurance that such insurance coverage is or will continue to be adequate or available to us at a cost acceptable to us or at all. We may choose or find it necessary under our collaborative agreements to increase our insurance coverage in the future. We may not be able to secure greater or broader product liability insurance coverage on acceptable terms or at reasonable costs when needed. Any liability for damages resulting from a product liability claim could exceed the amount of our coverage, require us to pay a substantial monetary award from our own cash resources and have a material adverse effect on our business, financial condition and results of operations. Moreover, a product recall, if required, could generate substantial negative publicity about our products and business and inhibit or prevent commercialization of

other products and drug candidates.

In addition, some of our licensing and other agreements with third parties require or might require us to maintain product liability insurance. If we cannot maintain acceptable amounts of coverage on commercially reasonable terms in accordance with the terms set forth in these agreements, the corresponding agreements would be subject to termination, which could have a material adverse impact on our operations.

Table of Contents

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them.

Because we rely on third parties to develop our products, we must share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs which may require us to share trade secrets under the terms of research and development partnership or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets would impair our competitive position.

We may not be able to successfully integrate newly-acquired technology with our existing technology or to modify our technologies to create new vaccines.

As part of our acquisition of technology assets from entities such as Amgen, we have acquired access to Fms-like tyrosine kinase 3 ligand, or Flt3L, which may improve the immunogenicity of our vaccines. If we are able to integrate these licensed assets with our vaccine technologies, we believe these assets will give our vaccines a competitive advantage. However, if we are unable to successfully integrate licensed assets, or other technologies which we have acquired or may acquire in the future, with our existing technologies and potential products currently under development, we may be unable to realize any benefit from our acquisition of these assets, or other technologies which we have acquired or may acquire in the future and may face the loss of our investment of financial resources and time in the integration process.

We believe that our vaccine technology portfolio may offer opportunities to develop vaccines that treat a variety of oncology, inflammatory and infectious diseases by stimulating a patient's immune system against those disease organisms. If our vaccine technology portfolio cannot be used to create effective vaccines against a variety of disease organisms, we may lose all or portions of our investment in development efforts for new vaccine candidates.

We license technology from other companies to develop products, and those companies could influence research and development or restrict our use of it.

Companies that license technologies to us that we use in our research and development programs may require us to achieve milestones or devote minimum amounts of resources to develop products using those technologies. They may also require us to make significant royalty and milestone payments, including a percentage of any sublicensing income, as well as payments to reimburse them for patent costs. The number and variety of our research and development programs require us to establish priorities and to allocate available resources among competing programs. From time to time we may choose to slow down or cease our efforts on particular products. If in doing so we fail to fully perform our obligations under a license, the licensor can terminate the licenses or permit our competitors to use the technology. Moreover, we may lose our right to market and sell any products based on the licensed technology.

Table of Contents

We have many competitors in our field and they may develop technologies that make ours obsolete.

Biotechnology, pharmaceuticals and therapeutics are rapidly evolving fields in which scientific and technological developments are expected to continue at a rapid pace. We have many competitors in the U.S. and abroad. The competitors for which we are aware have initiated a Phase 3 study or have obtained marketing approval for a potentially competitive drug include Alexion, Agenus, Baxter, BMS, Dendreon, Eli Lilly, GlaxoSmithKline, ImmunoGen, Merck, Pfizer, Roche, Sanofi-Aventis, Seattle Genetics, and Takeda. Our success depends upon our ability to develop and maintain a competitive position in the product categories and technologies on which we focus. Many of our competitors have greater capabilities, experience and financial resources than we do. Competition is intense and is expected to increase as new products enter the market and new technologies become available. Our competitors may:

develop technologies and products that are more effective than ours, making ours obsolete or otherwise noncompetitive;

obtain regulatory approval for products more rapidly or effectively than us; and

obtain patent protection or other intellectual property rights that would block our ability to develop competitive products.

We rely on patents, patent applications and other intellectual property protections to protect our technology and trade secrets; which are expensive and may not provide sufficient protection.

Our success depends in part on our ability to obtain and maintain patent protection for technologies that we use. Biotechnology patents involve complex legal, scientific and factual questions and are highly uncertain. To date, there is no consistent policy regarding the breadth of claims allowed in biotechnology patents, particularly in regard to patents for technologies for human uses like those we use in our business. We cannot predict whether the patents we seek will issue. If they do issue, a competitor may challenge them and limit their scope. Moreover, our patents may not afford effective protection against competitors with similar technology. A successful challenge to any one of our patents could result in a third party's ability to use the technology covered by the patent. We also face the risk that others will infringe, avoid or circumvent our patents. Technology that we license from others is subject to similar risks and this could harm our ability to use that technology. If we, or a company that licenses technology to us, were not the first creator of an invention that we use, our use of the underlying product or technology will face restrictions, including elimination.

If we must defend against suits brought against us or prosecute suits against others involving intellectual property rights, we will incur substantial costs. In addition to any potential liability for significant monetary damages, a decision against us may require us to obtain licenses to patents or other intellectual property rights of others on potentially unfavorable terms. If those licenses from third parties are necessary but we cannot acquire them, we would attempt to design around the relevant technology, which would cause higher development costs and delays, and may ultimately prove impracticable.

Our business requires us to use hazardous materials, which increases our exposure to dangerous and costly accidents.

Our research and development activities involve the use of hazardous chemicals, biological materials and radioactive compounds. Although we believe that our safety procedures for handling and disposing of hazardous materials comply with the standards prescribed by applicable laws and regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, an injured party will likely sue us for any resulting damages with potentially significant liability. The ongoing cost of complying with environmental laws and regulations is significant and may increase in the future.

Table of Contents

Health care reform and restrictions on reimbursement may limit our returns on potential products.

Because our strategy ultimately depends on the commercial success of our products, we assume, among other things, that end users of our products will be able to pay for them. In the United States and other countries, in most cases, the volume of sales of products like those we are developing depends on the availability of reimbursement from third-party payors, including national health care agencies, private health insurance plans and health maintenance organizations. Third-party payors increasingly challenge the prices charged for medical products and services. Accordingly, if we succeed in bringing products to market, and reimbursement is not available or is insufficient, we could be prevented from successfully commercializing our potential products.

The health care industry in the United States and in Europe is undergoing fundamental changes as a result of political, economic and regulatory influences. Reforms proposed from time to time include mandated basic health care benefits, controls on health care spending, the establishment of governmental controls over the cost of therapies, creation of large medical services and products purchasing groups and fundamental changes to the health care delivery system. We anticipate ongoing review and assessment of health care delivery systems and methods of payment in the United States and other countries. We cannot predict whether any particular reform initiatives will result or, if adopted, what their impact on us will be. However, we expect that adoption of any reform proposed will impair our ability to market products at acceptable prices and that uncertainty concerning future government regulation of consumer healthcare purchasing and insurance may result in difficulties for drug development companies, like us, in raising capital.

Changes in laws affecting the health care industry could adversely affect our business.

In the U.S., there have been numerous proposals considered at the federal and state levels for comprehensive reforms of health care and its cost, and it is likely that federal and state legislatures and health agencies will continue to focus on health care reform in the future. Congress has considered legislation to reform the U.S. health care system by expanding health insurance coverage, reducing health care costs and making other changes. While health care reform may increase the number of patients who have insurance coverage for our products, it may also include cost containment measures that adversely affect reimbursement for our products. Congress has also considered legislation to change the Medicare reimbursement system for outpatient drugs, increase the amount of rebates that manufacturers pay for coverage of their drugs by Medicaid programs and facilitate the importation of lower-cost prescription drugs that are marketed outside the U.S. Some states are also considering legislation that would control the prices of drugs, and state Medicaid programs are increasingly requesting manufacturers to pay supplemental rebates and requiring prior authorization by the state program for use of any drug for which supplemental rebates are not being paid. Managed care organizations continue to seek price discounts and, in some cases, to impose restrictions on the coverage of particular drugs. Government efforts to reduce Medicaid expenses may lead to increased use of managed care organizations by Medicaid programs. This may result in managed care organizations influencing prescription decisions for a larger segment of the population and a corresponding constraint on prices and reimbursement for our products.

We and our collaborators and partners operate in a highly regulated industry. As a result, governmental actions may adversely affect our business, operations or financial condition, including:

new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to health care availability, method of delivery and payment for health care products and services;

changes in the FDA and foreign regulatory approval processes that may delay or prevent the approval of new products and result in lost market opportunity;

changes in FDA and foreign regulations that may require additional safety monitoring, labeling changes, restrictions on product distribution or use, or other measures after the introduction of our

Table of Contents

products to market, which could increase our costs of doing business, adversely affect the future permitted uses of approved products, or otherwise adversely affect the market for our products;

new laws, regulations and judicial decisions affecting pricing or marketing practices; and

changes in the tax laws relating to our operations.

The enactment in the U.S. of health care reform, possible legislation which could ease the entry of competing follow-on biologics in the marketplace, new legislation or implementation of existing statutory provisions on importation of lower-cost competing drugs from other jurisdictions, and legislation on comparative effectiveness research are examples of previously enacted and possible future changes in laws that could adversely affect our business. In addition, the Food and Drug Administration Amendments Act of 2007 included new authorization for the FDA to require post-market safety monitoring, along with an expanded clinical trials registry and clinical trials results database, and expanded authority for the FDA to impose civil monetary penalties on companies that fail to meet certain commitments.

If physicians, patients and third-party payors do not accept any future drugs that we may develop, we may be unable to generate significant revenue, if any.

Even if our drug candidates as well as any drug candidates that we may develop or acquire in the future obtain regulatory approval, they may not gain market acceptance among physicians, patients and health care payors. Physicians may elect not to recommend these drugs for a variety of reasons including:

timing of market introduction of competitive drugs;
lower demonstrated clinical safety and efficacy compared to other drugs;
lack of cost-effectiveness;
lack of availability of reimbursement from third-party payors;
convenience and ease of administration;
prevalence and severity of adverse side effects;
other potential advantages of alternative treatment methods; and
ineffective marketing and distribution support.

If any drugs that we may develop fail to achieve market acceptance, we would not be able to generate sufficient revenue from product sales to maintain or grow our business.

The restrictive covenants contained in our credit agreement may limit our activities.

On December 30, 2010, we entered into a Loan and Security Agreement (the "Loan Agreement") with MidCap Financial, LLC (MidCap) pursuant to which we borrowed \$10 million (the "Term Loan") from MidCap. In March 2011, we amended the Loan Agreement and borrowed

an additional \$5 million from General Electric Capital Corporation (GECC) (collectively with MidCap, the "Lenders") to increase the amount owed under the Term Loan to \$15 million. In March 2012, we amended the Loan Agreement to extend the maturity date from December 2013 to December 2014 in return for an upfront fee of \$25,000 and an additional fee of \$37,500 due upon repayment of the Term Loan in full. Our obligations under the Term Loan are secured by a first priority lien upon and security interest in substantially all of our existing and after-acquired assets, excluding our intellectual property assets (the "Collateral"). Under the Term Loan, we are subject to specified affirmative covenants customary for loans of this type, including but not limited to the obligations to maintain good standing, provide various notices to the Lenders, deliver financial statements to the Lenders, maintain adequate insurance, promptly discharge all taxes, protect our intellectual property and protect the Collateral. We are also subject to certain negative covenants customary for loans of this type, including but not limited to prohibitions against certain mergers and consolidations, certain management and ownership changes constituting a "change of control," and the imposition of additional liens on Collateral or other of our assets, as well as prohibitions against additional indebtedness, certain dispositions of property, changes in our business, name or location, payment of dividends,

Table of Contents

prepayment of certain other indebtedness, certain investments or acquisitions, and certain transactions with affiliates, in each case subject to certain customary exceptions, including exceptions that allow us to enter into non-exclusive and/or exclusive licenses and similar agreements providing for the use of our intellectual property in collaboration with third parties provided certain conditions are met.

Failure to comply with the restrictive covenants in our Term Loan could accelerate the repayment of any debt outstanding under the Term Loan. Additionally, as a result of these restrictive covenants, we may be at a disadvantage compared to our competitors that have greater operating and financing flexibility than we do.

Our ability to use our net operating loss carryforwards will be subject to limitation and, under certain circumstances, may be eliminated.

Utilization of our net operating loss, or NOL, and research and development credit carryforwards may be subject to substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future provided by Section 382 of the Internal Revenue Code of 1986, or Section 382, as well as similar state provisions. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period.

In October 2007, June 2009 and in December 2009, we experienced a change in ownership as defined by Section 382 of the Internal Revenue Code. Historically, we have raised capital through the issuance of capital stock on several occasions which, combined with shareholders' subsequent disposition of those shares, has resulted in three changes of control, as defined by Section 382. As a result of the ownership change in October 2007, utilization of its Federal NOLs is subject to an annual limitation. Any unused annual limitation may be carried over to later years, and the amount of the limitation may, under certain circumstances, be subject to adjustment if the fair value of the our net assets are determined to be below or in excess of the tax basis of such assets at the time of the ownership change, and such unrealized loss or gain is recognized during the five-year period after the ownership change. Subsequent ownership changes, as defined in Section 382, could further limit the amount of net operating loss carryforwards and research and development credits that can be utilized annually to offset future taxable income.

We have not undertaken a study to assess whether an ownership change or multiple ownership changes has occurred for (i) AVANT or CuraGen prior to our acquisitions, (ii) the Company on the state level, (iii) the Company since October 2012, or (iv) research and development credits. If, based on such a study, we were to determine that there has been an ownership change at any time since its formation, utilization of NOL or tax credit carryforwards would be subject to an annual limitation under Section 382.

Risks Related to this Offering

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Because we have not designated the amount of net proceeds from this offering to be used for any particular purpose, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of the offering. Our management may use the net proceeds for corporate purposes that may not improve our financial condition or market value.

Table of Contents

You will experience immediate and substantial dilution in the book value per share of the common stock you purchase.

Because the price per share of our common stock being offered may be higher than the book value per share of our common stock, you may suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. See the section entitled "Dilution" below for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering. In addition, we have a significant number of options and restricted stock outstanding. If the holders of these securities exercise or convert them or become vested in them, as applicable, you may incur further dilution.

Sales of a significant number of shares of our common stock in the public markets could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock or other equity-related securities in the public markets could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We cannot predict the effect that future sales of our common stock or other equity-related securities would have on the market price of our common stock. Under the terms of the Cantor Agreement, we will have the ability to sell an amount of shares of common stock having an aggregate offering price of up to \$4.4 million upon the expiration or earlier waiver of our 90-day lock-up with the underwriters of this offering. We cannot predict the effect that future sales of our common stock or other equity related securities will have on the market price of our common stock.

Our share price has been and could remain volatile.

The market price of our common stock has historically experienced and may continue to experience significant volatility. During 2012, our common stock traded as low as \$2.65 and as high as \$7.20. Our progress in developing and commercializing our products, the impact of government regulations on our products and industry, the potential sale of a large volume of our common stock by stockholders, our quarterly operating results, changes in general conditions in the economy or the financial markets and other developments affecting us or our competitors could cause the market price of our common stock to fluctuate substantially with significant market losses. If our stockholders sell a substantial number of shares of common stock, especially if those sales are made during a short period of time, those sales could adversely affect the market price of our common stock and could impair our ability to raise capital. In addition, in recent years, the stock market has experienced significant price and volume fluctuations. This volatility has affected the market prices of securities issued by many companies for reasons unrelated to their operating performance and may adversely affect the price of our common stock. In addition, we could be subject to a securities class action litigation as a result of volatility in the price of our stock, which could result in substantial condition.

Table of Contents

Special Note Regarding Forward-Looking Statements

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein contain forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements represent our management's judgment regarding future events. In many cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "plan," "expect," "anticipate," "estimate," "predict," "intend," "potential" or "continue" or the negative of these terms or other words of similar import, although some forward-looking statements are expressed differently. All statements other than statements of historical fact included in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein regarding our financial position, business strategy and plans or objectives for future operations are forward-looking statements. Without limiting the broader description of forward-looking statements above, we specifically note that statements regarding potential drug candidates, their potential therapeutic effect, the possibility of obtaining regulatory approval, our expected timing for completing clinical trials and clinical trial milestones for our drug candidates, our ability or the ability of our collaborators to manufacture and sell any products, market acceptance or our ability to earn a profit from sales or licenses of any drug candidate or to discover new drugs in the future are all forward-looking in nature. We cannot guarantee the accuracy of forward-looking statements, and you should be aware that results and events could differ materially and adversely from those described in the forward-looking statements due to a number of factors, including:

our ability to raise sufficient capital to fund our clinical studies, including our registration studies for rindopepimut which we estimate will cost over \$60 million, and to meet our long-term liquidity needs, on terms acceptable to us, or at all;

our ability to successfully complete research and further development, including animal, preclinical and clinical studies, and commercialization of rindopepimut, CDX-011, CDX-1127, and other product candidates and the growth of the markets for those drug candidates;

our ability to manage multiple clinical trials for a variety of drug candidates at different stages of development, including our Phase 3 trial for rindopepimut;

the cost, timing, scope and results of ongoing safety and efficacy trials of rindopepimut, CDX-011, CDX-1127 and other preclinical and clinical testing;

our ability to fund and complete the development and commercialization of rindopepimut for North America internally and to find a strategic partner to commercialize rindopepimut outside North America;

the ability to negotiate strategic partnerships, where appropriate, for our lead programs, including CDX-011 and CDX-1127, as well as for our non-core programs;

our ability to adapt our APC Targeting Technology to develop new, safe and effective vaccines against oncology and infectious disease indications;

our ability to develop technological capabilities and expand our focus to broader markets for vaccines;

the availability, cost, delivery and quality of clinical and commercial grade materials produced by our own manufacturing facility or supplied by contract manufacturers and partners;

the availability, cost, delivery and quality of clinical management services provided by our clinical research organization partners;

the timing, cost and uncertainty of obtaining regulatory approvals for our drug candidates;

our ability to develop and commercialize products before competitors that are superior to the alternatives developed by such competitors; and

the validity of our patents and our ability to avoid intellectual property litigation, which can be costly and divert management time and attention.

Table of Contents

You should also consider carefully the statements set forth in the section entitled "Risk Factors" in this prospectus supplement, as may be updated by any other document that we subsequently filed with the Securities and Exchange Commission and that is incorporated by reference into this prospectus supplement, which address various factors that could cause results or events to differ from those described in the forward-looking statements. All subsequent written and oral forward-looking statements attributable to us or to persons acting on our behalf are expressly qualified in their entirety by the applicable cautionary statements. We have no plans to update these forward-looking statements.

Table of Contents

Use of Proceeds

We estimate that the net proceeds from this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately \$, or approximately \$, if the underwriters exercise their option to purchase additional shares in full. We currently expect to use the net proceeds from this offering to fund clinical trials of our product candidates and for working capital and other general corporate purposes. Until we use the net proceeds of this offering, we intend to invest the funds in short-term, investment grade, interest-bearing securities.

The amount and timing of actual expenditures for the purposes set forth above may vary based on several factors, and our management will retain broad discretion as to the ultimate allocation of the proceeds.

Table of Contents

Dilution

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share and our pro forma net tangible book value per share after this offering. We calculate net tangible book value per share by dividing our net tangible book value, which is tangible assets less total liabilities, by the number of outstanding shares of our common stock.

Our net tangible book value as of September 30, 2012 was approximately \$58.0 million, or \$0.95 per share. After giving effect to the sale by us of shares of common stock offered by this prospectus supplement at a public offering price of \$ per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma net tangible book value as of September 30, 2012 would have been approximately \$ million, or \$ per share. This represents an immediate increase in pro forma net tangible book value of \$ per share to existing stockholders and an immediate dilution of \$ per share to new investors purchasing our common stock in this offering. The following table illustrates the per share dilution:

Public offering price per share		\$
Net tangible book value per share as of September 30, 2012	\$ 0.95	
Increase in net tangible book value per share after this offering	\$	
Pro forma net tangible book value per share as of September 30, 2012, after giving effect to this offering		\$
Dilution per share to new investors in this offering		\$

The information above assumes that the underwriters do not exercise their option to purchase additional shares. If the underwriters exercise their option to purchase additional shares in full, our pro forma net tangible book value per share at September 30, 2012 after giving effect to this offering would have been \$ per share, and the dilution in pro forma net tangible book value per share to investors in this offering would have been \$ per share. The above discussion and table are based on 60,807,350 shares of our common stock issued and outstanding as of September 30, 2012, which does not include the following:

5,351,999 shares issuable upon the exercise of outstanding stock options as of September 30, 2012 with a weighted-average exercise price of \$5.97 per share;

3,380,865 shares available for future issuance under our equity compensation plans as of September 30, 2012; and

5,954,798 shares of common stock issued after September 30, 2012 through February 1, 2013 which raised \$38.0 million in net proceeds.

Table of Contents

Underwriting

Subject to the terms and conditions set forth in the underwriting agreement, dated February , 2013, between us, and Jefferies & Company, Inc. and Leerink Swann LLC, as the representatives of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

Underwriter	Number of Shares
Chuci writer	Shares
Jefferies & Company, Inc.	
Leerink Swann LLC	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ per share of common stock. The underwriters may allow, and certain dealers may reallow, a discount from the concession not in excess of \$ per share of common stock to certain brokers and dealers. After the offering, the initial public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such

Table of Contents

amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Per Share		To	otal
	Without	With	Without	With
	Option to	Option to	Option to	Option to
	Purchase	Purchase	Purchase	Purchase
	Additional	Additional	Additional	Additional
	Shares	Shares	Shares	Shares
Public offering price	\$	\$	\$	\$
Underwriting discounts and commissions paid				
by us	\$	\$	\$	\$
Proceeds to us, before expenses	\$	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of \$11,250,000 from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above.

No Sales of Similar Securities

We, our officers, directors and holders of all or substantially all our outstanding capital stock have agreed, subject to specified exceptions, not to directly or indirectly:

sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, or

otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or

publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus without the prior written consent of Jefferies & Company, Inc.

This restriction terminates after the close of trading of the common stock on and including the 90th day after the date of this prospectus. However, subject to certain exceptions, in the event that either:

during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to us occurs, or

prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day restricted period,

then in either case the expiration of the 90-day restricted period will be extended until the expiration of the 18-day period beginning on the date of the issuance of an earnings release or the occurrence of the material news or event, as applicable, unless Jefferies & Company, Inc. waives, in writing, such an extension.

Jefferies & Company, Inc. may, in its sole discretion and at any time or from time to time before the termination of the 90-day period, release all or any portion of the securities subject to lock-up agreements.

Table of Contents

There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that they, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

"Naked" short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriter's purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on The NASDAQ Global Select Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Table of Contents

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriter and certain of its affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriter and certain of its affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriter and certain of its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Table of Contents

Notice to Investors

Australia

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

You confirm and warrant that you are either:

- a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or
- a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus for resale in Australia within 12 months of those shares being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the "Relevant Implementation Date"), no offer of any securities which are the subject of the offering contemplated by this prospectus has been or will be made to the public in that Relevant Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the relevant competent authority in that Relevant Member State in accordance with the Prospectus Directive, except that with effect from and including the Relevant Implementation Date, an offer of such securities may be made to the public in that Relevant Member State:

- (a) to any legal entity which is a "qualified investor" as defined in the Prospectus Directive;
- (b)
 to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives of the underwriters for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of securities shall require the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable

an investor to decide to purchase or subscribe the securities, as the same may be varied in that Relevant Member State by any measure

S-30

Table of Contents

implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be insued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the Initial Purchaser will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

S-31

Table of Contents

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b)
 a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor.

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:

- (i)
 to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;
- (ii) where no consideration is given for the transfer; or
- (iii) where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX") or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA ("FINMA"), and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated (each such person being referred to as a "relevant person").

Table of Contents

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Legal Matters

Lowenstein Sandler LLP, Roseland, New Jersey, will provide us with an opinion as to the validity of the shares of common stock offered by this prospectus supplement and the accompanying prospectus. This opinion may be conditioned upon and may be subject to assumptions regarding future actions required to be taken by us and any underwriters, dealers or agents in connection with the issuance and sale of the securities. Covington & Burling LLP, New York, New York, is counsel for the underwriters in connection with this offering.

Experts

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2011 have been so incorporated in reliance on the report(s) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

Where You Can Find More Information

We file annual, quarterly and current reports, proxy statements and other information with the SEC. We have also filed a registration statement on Form S-3, including exhibits, under the Securities Act with respect to the securities offered by this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus are a part of the registration statement but do not contain all of the information included in the registration statement or the exhibits. You may read and copy the registration statement and any other document that we file at the SEC's public reference room at 100 F Street, N.E., Room 1580, Washington D.C. 20549. You can call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference room. You can also find our public filings with the SEC on the Internet at a web site maintained by the SEC located at http://www.sec.gov.

Table of Contents

Incorporation of Documents by Reference

The SEC allows us to "incorporate by reference" information from other documents that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus supplement and the accompanying prospectus, and information that we file later with the SEC will automatically update and supersede this information. We filed a registration statement on Form S-3 under the Securities Act with the SEC with respect to the securities being offered pursuant to this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus omit certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the common stock being offered pursuant to this prospectus supplement. Statements in this prospectus supplement and the accompanying prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in "Where You Can Find More Information." The documents we are incorporating by reference are:

- (a) Our Annual Report on Form 10-K for the fiscal year ended December 31, 2011, filed on March 8, 2012;
- (b) Our Quarterly Reports on Form 10-Q for the quarterly periods ending March 31, 2012, filed on May 4, 2012, June 30, 2012, filed on August 9, 2012, and September 30, 2012, filed on November 2, 2012;
- (c)
 Our Current Reports on Form 8-K filed on February 23, 2012, February 24, 2012, March 7, 2012, April 3, 2012, June 14, 2012, September 24, 2012, December 21, 2012 and February 4, 2013; and
- (d)

 The description of our common stock contained in our Registration Statement on Form 8-A, filed on November 8, 2004, as amended by Form 8-A/A filed on October 22, 2007 and March 7, 2008.

In addition, all documents subsequently filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, before the date our offering is terminated or complete (other than any portion of such filings that are furnished under applicable SEC rules rather than filed), are deemed to be incorporated by reference into, and to be a part of, this prospectus supplement and the accompanying prospectus.

You may request a copy of these filings, at no cost, by writing to or telephoning us at the following address:

Corporate Secretary
Celldex Therapeutics, Inc.
119 Fourth Avenue
Needham, Massachusetts 02494
(781) 433-0771

Any statement contained in this prospectus supplement or in a document incorporated or deemed to be incorporated by reference into this prospectus supplement will be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus supplement modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

Table of Contents

You should rely only on information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus supplement and the accompanying prospectus or incorporated by reference in this prospectus supplement and the accompanying prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

S-35

Table of Content
PROSPECTUS

CELLDEX THERAPEUTICS, INC.

\$200,000,000 Common Stock Preferred Stock Warrants Depositary Shares Units

Celldex Therapeutics, Inc. may offer, issue and sell from time to time, together or separately, in one or more offerings, any combination of:

our common stock,

our preferred stock, which we may issue in one or more series,

warrants,

depositary shares, and

units,

up to a maximum aggregate offering price of \$200,000,000.

This prospectus provides a general description of the securities we may offer. Each time we sell securities, we will provide specific terms of the securities offered in a supplement to this prospectus (which includes an at-the-market offering prospectus). The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and the accompanying prospectus supplement, as well as the documents incorporated or deemed incorporated by reference in this prospectus, carefully before you make your investment decision. Our common stock is traded on the NASDAQ Global Market under the symbol "CLDX." On December 18, 2012, the last reported sale price of our common stock on the NASDAQ Global Market was \$6.64 per share. You are urged to obtain current market quotations of the common stock. Each prospectus supplement will indicate if the securities offered thereby will be listed on any securities exchange.

This prospectus may not be used to sell securities unless accompanied by a prospectus supplement.

We may offer to sell these securities on a continuous or delayed basis, through agents, dealers or underwriters, or directly to purchasers. The prospectus supplement for each offering of securities will describe in detail the plan of distribution for that offering. If our agents or any dealers or underwriters are involved in the sale of the securities, the applicable prospectus supplement will set forth the names of the agents, dealers or underwriters and any applicable commissions or discounts. Our net proceeds from the sale of securities will also be set forth in the applicable prospectus supplement. For general information about the distribution of securities offered, please see "Plan of Distribution" in this prospectus.

Investing in our securities involves risks. Before making an investment decisions, you should carefully review the information contained in this prospectus under the heading "Risk Factors" beginning on page 4 of this prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION OR REGULATORY BODY HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is January 4, 2013.

Table of Contents

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS	<u>1</u>
PROSPECTUS SUMMARY	<u>2</u>
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	<u>4</u>
RISK FACTORS	<u>4</u>
RATIOS OF COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS TO EARNINGS	<u>5</u>
<u>USE OF PROCEEDS</u>	<u>5</u>
DESCRIPTIONS OF SECURITIES WE MAY OFFER	<u>5</u>
<u>DESCRIPTION OF COMMON STOCK</u>	<u>6</u>
DESCRIPTION OF PREFERRED STOCK	7
<u>DESCRIPTION OF WARRANTS</u>	<u>9</u>
<u>DESCRIPTION OF DEPOSITARY SHARES</u>	<u>11</u>
<u>DESCRIPTION OF UNITS</u>	<u>12</u>
<u>PLAN OF DISTRIBUTION</u>	<u>12</u>
<u>LEGAL MATTERS</u>	<u>14</u>
<u>EXPERTS</u>	<u>14</u>
WHERE YOU CAN FIND MORE INFORMATION	<u>14</u>
INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE	<u>15</u>

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may, from time to time, sell any combination of the securities described in this prospectus in one or more offerings.

The registration statement containing this prospectus, including the exhibits to the registration statement, provides additional information about us and the securities offered under this prospectus. You should read the registration statement and the accompanying exhibits for further information. The registration statement, including the exhibits and the documents incorporated or deemed incorporated herein by reference, can be read and are available to the public over the Internet at the SEC's website at http://www.sec.gov as described under the heading "Where You Can Find More Information."

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities pursuant to this prospectus, we will provide a prospectus supplement (which term includes, as applicable, the at-the-market offering prospectus filed with the registration statement of which this prospectus forms a part) containing specific information about the terms of a particular offering by us. That prospectus supplement may include a discussion of any risk factors or other special considerations that apply to those securities. The prospectus supplement may add, update or change information in this prospectus. If the information in the prospectus is inconsistent with a prospectus supplement, you should rely on the information in that prospectus supplement. You should read both this prospectus and, if applicable, any prospectus supplement. See "Where You Can Find More Information" for more information.

You should rely only on the information incorporated by reference or provided in this prospectus. We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus or any prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or any prospectus supplement. This prospectus and any prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and any prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus or any prospectus supplement is accurate on any date subsequent to the date set forth on the front of such document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any prospectus supplement is delivered or securities are sold on a later date.

Unless this prospectus indicates otherwise or the context otherwise requires, the terms "we," "our," "us," "Celldex" or the "Company" as used in this prospectus refer to Celldex Therapeutics, Inc. and its subsidiaries, except that such terms refer to only Celldex Therapeutics, Inc. and not its subsidiaries in the sections entitled "Description of Common Stock," "Description of Preferred Stock," "Description of Warrants," "Description of Depositary Shares," and "Description of Units."

Table of Contents

PROSPECTUS SUMMARY

Company Overview

We are a biopharmaceutical company focused on the development and commercialization of several immunotherapy technologies for the treatment of cancer and other difficult-to-treat diseases. Our lead drug candidates include rindopepimut (CDX-110), an immunotherapeutic vaccine in a pivotal Phase 3 study for the treatment of front-line glioblastoma and a Phase 2 study for the treatment of recurrent glioblastoma, CDX-011, an antibody-drug conjugate which recently completed a randomized Phase 2b study for the treatment of advanced breast cancer and CDX-1127, a therapeutic human antibody in a Phase 1 study for cancer indications. We have additional clinical and preclinical programs, including CDX-1401, an APC Targeting Technology program, CDX-301, an immune cell mobilizing agent and dendritic cell growth factor and CDX-1135, a molecule that inhibits a part of the immune system called the complement system. Our drug candidates address market opportunities for which we believe current therapies are inadequate or non-existent.

Generally our strategy is to develop and demonstrate proof-of-concept for our drug candidates before leveraging their value through partnerships or, in appropriate situations, continuing late stage development through commercialization ourselves. Demonstrating proof-of-concept for a drug candidate generally involves bringing it through Phase 1 clinical trials and one or more Phase 2 clinical trials so that we are able to demonstrate, based on human trials, good safety data for the drug candidate and some data indicating its effectiveness. We thus leverage the value of our technology portfolio through corporate, governmental and non-governmental partnerships. This approach allows us to maximize the overall value of our technology and product portfolio while best ensuring the expeditious development of each individual product. Our current collaborations include the commercialization of an oral human rotavirus vaccine. We are exploring potential development and commercialization collaborations for certain drug candidates such as CDX-011 and CDX-1127. Furthermore, while we plan to retain the rights to develop and commercialize rindopepimut in North America, we are exploring potential partnership opportunities to commercialize rindopepimut outside of North America.

Our products are derived from a broad set of complementary technologies which have the ability to utilize the human immune system and enable the creation of therapeutic agents. We are using these technologies to develop targeted immunotherapeutics comprised of antibodies, adjuvants and monotherapies and antibody-drug conjugates that prevent or treat cancer and other diseases that modify undesirable activity by the body's own proteins or cells. A number of our immunotherapeutic and antibody-drug conjugate drug candidates are in various stages of clinical trials. We expect that a large percentage of our research and development expenses will be incurred in support of our current and future clinical trial programs.

Rindopepimut (CDX-110)

Rindopepimut is an immunotherapeutic vaccine that targets the tumor-specific molecule, epidermal growth factor receptor variant III, or EGFRvIII. EGFRvIII is a mutated form of the epidermal growth factor receptor, or EGFR, that is only expressed in cancer cells and not in normal tissue and can directly contribute to cancer cell growth. EGFRvIII is expressed in approximately 30% of glioblastoma, or GB, tumors the most common and aggressive form of brain cancer. The rindopepimut vaccine is composed of the EGFRvIII peptide linked to a carrier protein called Keyhole Limpet Hemocyanin, or KLH, and administered together with the adjuvant GM-CSF. The Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA, have both granted orphan drug designation for rindopepimut for the treatment of EGFRvIII expressing GB and the FDA has also granted Fast Track designation.

Table of Contents

Glembatumumab Vedotin (CDX-011)

CDX-011 is an antibody-drug conjugate for the treatment of patients with glycoprotein NMB, or GPNMB, expressing advanced, refractory breast cancer. CDX-011 targets the protein GPNMB, which is over expressed in a variety of cancers, including breast cancer and melanoma. The FDA has granted Fast Track designation to CDX-011 for the treatment of advanced, refractory/resistant GPNMB-expressing breast cancer.

CDX-1127

CDX-1127 is a human monoclonal antibody that targets CD27, a potentially important target for immunotherapy of various cancers. CD27 acts downstream from CD40 and may provide a novel way to regulate the immune responses. CD27 is a co-stimulatory molecule on T cells and is over-expressed in certain lymphomas and leukemias. CDX-1127 is an agonist antibody designed to have two potential therapeutic mechanisms. CDX-1127 has been shown to activate immune cells that can target and eliminate cancerous cells in tumor-bearing mice and to directly kill or inhibit the growth of CD27-expressing lymphomas and leukemias in vitro and in vivo. Both mechanisms have been seen even at low doses in preclinical models.

Other Clinical and Pre-Clinical Programs

We have several other programs in clinical and pre-clinical development. The status of the other programs that we currently believe are material to our business is summarized in the table below:

Product Candidate	Indication/Field	Stage of Clinical Development
CDX-1401	Multiple solid tumors	Phase 1
CDX-301	Cancer, autoimmune disease and transplant	Phase 1
CDX-1135	Renal disease	Preclinical

Rotarix

In 1997, we licensed our oral rotavirus strain to GlaxoSmithKline plc, or Glaxo, and Glaxo assumed responsibility for all subsequent clinical trials and all other development activities. We licensed-in the rotavirus strain that was used to develop Glaxo's Rotarix rotavirus vaccine in 1995 and owe a license fee of 30% to Cincinnati Children's Hospital Medical Center, or CCH, on net royalties received from Glaxo. In May 2005, we entered into an agreement whereby an affiliate of Paul Royalty Fund II, L.P., or PRF, purchased a 70% interest in the net royalties we received on worldwide sales of Rotarix.

In December 2012, a U.S. patent for our rotavirus strain that we licensed to Glaxo expired. The Glaxo agreement expires upon the expiration, lapse or invalidation of the last relevant patent right (patent or patent application) covered by the Glaxo agreement, although Glaxo may terminate the agreement upon 90 days prior written notice. A patent application in Mexico with a projected final expiry date in May 2013 is under appeal. The PRF agreement provided for a normal expiry of the PRF agreement on December 12, 2012 except that the PRF agreement stays in effect until PRF receives their final royalty payment. In addition, the PRF agreement provides for an exclusive 120-day right of negotiation for extension in certain circumstances.

Corporate Information

We are a Delaware corporation organized in 1983. On October 1, 2009, a wholly-owned subsidiary of Celldex merged with and into CuraGen Corporation. On December 31, 2009, CuraGen Corporate was merged with and into Celldex and the separate existence of CuraGen ceased.

Table of Contents

Our principal executive offices are located at 119 Fourth Avenue, Needham, Massachusetts 02494 and our telephone number is (781) 433-0771. Our corporate website is www.celldextherapeutics.com. The information on our website is not incorporated by reference into this prospectus.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but not always, made through the use of words or phrases such as "anticipate," "estimate," "plans," "projects," "continuing," "ongoing," "expects," "management believes," "we believe," "we intend" and similar words or phrases. Accordingly, these statements involve estimates, assumptions and uncertainties, which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the risk factors discussed in this prospectus or discussed in documents incorporated by reference in this prospectus.

Forward-looking statements are subject to known and unknown risks and uncertainties, which change over time, and are based on management's expectations and assumptions at the time the statements are made, and are not guarantees of future results. Our actual results may differ materially from those expressed or anticipated in the forward-looking statements for many reasons including the factors described in the section entitled "Risk Factors" in this prospectus and in any risk factors described in a supplement to this prospectus or in other filings.

You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date on which they were made. We undertake no obligation to publicly revise any forward-looking statement to reflect circumstances or events after the date of this prospectus or to reflect the occurrence of unanticipated events. You should, however, review the factors and risks we describe in the reports we file from time to time with the SEC after the date of this prospectus. We undertake no obligation to revise or update the forward-looking statements contained in this prospectus at any time. All forward-looking statements are qualified in their entirety by this cautionary statement.

RISK FACTORS

Investing in our securities involves significant risks. Before making an investment decision, you should carefully consider the risks and other information we include or incorporate by reference in this prospectus and any prospectus supplement. In particular, you should consider the risk factors under the heading "Risk Factors" included in our most recent Annual Report on Form 10-K, as may be revised or supplemented by our subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, each of which are on file with the SEC and are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not currently known to us or that we currently deem immaterial may also affect our business operations. Additional risk factors may be included in a prospectus supplement relating to a particular offering of securities. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our securities could decline due to any of these risks, and you may lose all or part of your investment. This prospectus is qualified in its entirety by these risk factors.

Table of Contents

RATIOS OF COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS TO EARNINGS

The following table sets forth our consolidated ratios of earnings to combined fixed charges and preferred stock dividends for the years ended December 31, 2011, 2010, 2009, 2008 and 2007. We do not have any outstanding shares of preferred stock and therefore have not paid any preferred stock dividends.

Ratios of Combined Fixed Charges

	Years ended December 31,					
2	2011	2010	2009	2008	2007	
	(1)	(1)	(1)	(1)	(1)	

Due to our losses from continuing operations for the years ended December 31, 2011, 2010, 2009, 2008 and 2007 earnings were insufficient to cover fixed charges by \$43.4 million, \$6.5 million, \$36.9 million, \$48.8 million, and \$15.5 million, respectively. For this reason, no ratios are provided.

USE OF PROCEEDS

Unless otherwise provided in the applicable prospectus supplement to this prospectus used to offer specific securities, we expect to use the net proceeds from any offering of securities by us for general corporate purposes, which may include acquisitions, capital expenditures, investments, and the repayment, redemption or refinancing of all or a portion of any indebtedness or other securities outstanding at a particular time, to fund our operations until we receive FDA approval of our products and are able to commercialize our products and to make substantial investments to establish sales, marketing, quality control, and regulatory compliance capabilities in anticipation of FDA approval of our products. Pending the application of the net proceeds, we expect to invest the net proceeds in short-term, interest-bearing instruments with a maturity of three months or less at the date of purchase and consist primarily of investments in money market mutual funds with commercial banks and financial institutions or other investment-grade securities. Such investments may include depositing such net proceeds into, and maintaining cash balances with, financial institutions in excess of insured limits.

DESCRIPTIONS OF SECURITIES WE MAY OFFER

This prospectus contains summary descriptions of the common stock, preferred stock, warrants, depositary shares and units that we may offer and sell from time to time. The preferred stock may also be exchangeable for and/or convertible into shares of common stock or another series of preferred stock. When one or more of these securities are offered in the future, a prospectus supplement will explain the particular terms of the securities and the extent to which these general provisions may apply. These summary descriptions and any summary descriptions in the applicable prospectus supplement do not purport to be complete descriptions of the terms and conditions of each security and are qualified in their entirety by reference to our third restated certificate of incorporation, as amended, our by-laws and by applicable Delaware law and any other documents referenced in such summary descriptions and from which such summary descriptions are derived. If any particular terms of a security described in the applicable prospectus supplement differ from any of the terms described herein, then the terms described herein will be deemed superseded by the terms set forth in that prospectus supplement.

Table of Contents

We may issue securities in book-entry form through one or more depositaries, such as The Depository Trust Company, Euroclear or Clearstream, named in the applicable prospectus supplement. Each sale of a security in book-entry form will settle in immediately available funds through the applicable depositary, unless otherwise stated. We will issue the securities only in registered form, without coupons, although we may issue the securities in bearer form if so specified in the applicable prospectus supplement. If any securities are to be listed or quoted on a securities exchange or quotation system, the applicable prospectus supplement will say so.

DESCRIPTION OF COMMON STOCK

As of December 18, 2012 we are authorized to issue up to 297,000,000 shares of common stock, \$.001 par value per share. As of December 18, 2012, approximately 63,682,919 shares of common stock were outstanding. All outstanding shares of our common stock are fully paid and non-assessable. Our common stock is listed on the NASDAQ Global Market under the symbol "CLDX."

Dividends

The Board of Directors may, out of funds legally available, at any regular or special meeting, declare dividends to the holders of shares of our common stock as and when they deem expedient, subject to the rights of holders of the preferred stock, if any.

Voting

Each share of common stock entitles the holders to one vote per share on all matters requiring a vote of the stockholders, including the election of directors. No holders of shares of common stock shall have the right to vote such shares cumulatively in any election for the board of directors.

Rights Upon Liquidation

In the event of our voluntary or involuntary liquidation, dissolution, or winding up, the holders of our common stock will be entitled to share equally in our assets available for distribution after payment in full of all debts and after the holders of preferred stock, if any, have received their liquidation preferences in full.

Miscellaneous

No holders of shares of our common stock shall have any preemptive rights to subscribe for, purchase or receive any shares of any class, whether now or hereafter authorized, or any options or warrants to purchase any such shares, or any securities convertible into or exchanged for any such shares, which may at any time be issued, sold or offered for sale by Celldex.

Anti-Takeover Provisions

Certain provisions in our third restated certificate of incorporation, as amended, and applicable Delaware corporate, as well as our shareholder rights agreement, may have the effect of discouraging a change of control of Celldex, even if such a transaction is favored by some of our stockholders and could result in stockholders receiving a substantial premium over the current market price of our shares. The primary purpose of these provisions is to encourage negotiations with our management by persons interested in acquiring control of our corporation. These provisions may also tend to perpetuate present management and make it difficult for stockholders owning less than a majority of the shares to be able to elect even a single director.

Pursuant to our shareholder rights agreement (referred to in this prospectus as the rights agreement) a dividend of one Preferred Stock Purchase Right (referred to in this prospectus as a right)

Table of Contents

for each share of common stock of Celldex was declared for each outstanding share of common stock of Celldex on November 11, 2004. Each share of common stock of Celldex issued after such date is also issued with a right. Each right entitles the registered holder to purchase from Celldex a unit consisting of one one-ten thousandth of a share of Celldex Series C-1 Junior Participating Cumulative Preferred Stock, at a cash exercise price of \$35 per unit, subject to adjustment as specified in the rights agreement. We describe the rights more completely in the rights agreement itself, which is contained in Exhibit 4.1 to our Registration Statement on Form 8-A filed on November 8, 2004. The summary of the provisions of the rights agreement is qualified in its entirety by reference to that agreement.

Computershare Trust Company, N.A. is presently the transfer agent and registrar for our common stock.

DESCRIPTION OF PREFERRED STOCK

At September 30, 2012, the Company had authorized preferred stock comprised of 3,000,000 shares of Class C Preferred Stock of which 350,000 shares has been designated as Class C-1 Junior Participating Cumulative Preferred Stock, the terms of which are to be determined by our Board of Directors. As of December 18, 2012, there was no preferred stock outstanding.

Class C Preferred Stock

This section describes the general terms and provisions of our Class C Preferred Stock. The applicable prospectus supplement will describe the specific terms of the shares of preferred stock offered through that prospectus supplement, as well as any general terms described in this section that will not apply to those shares of preferred stock.

Our board of directors has been authorized to provide for the issuance of the 2,650,000 unissued and undesignated shares of our Class C Preferred Stock In general, our third restated certificate of incorporation, as amended, authorizes our board of directors to issue new shares of our common stock or preferred stock without further stockholder action, provided that there are sufficient authorized shares.

With respect to each series of our Class C Preferred Stock, our board of directors has the authority to fix the following terms:

any restrictions on issuance of shares in the same series or any other series;

the designation of the series;

the number of shares within the series;

whether dividends are cumulative and, if cumulative, the dates from which dividends are cumulative;

the rate of any dividends, any conditions upon which dividends are payable, and the dates of payment of dividends;

whether interests in the shares of preferred stock will be represented by depositary shares as more fully described below under "Description of Depositary Shares";

whether the shares are redeemable, the redemption price and the terms of redemption;

the amount payable to you for each share you own if we dissolve or liquidate;

whether the shares are convertible or exchangeable, the price or rate of conversion or exchange, and the applicable terms and conditions;

Table of Contents

voting rights applicable to the series of preferred stock; and

any other rights, priorities, preferences, restrictions or limitations of such series.

The rights with respect to any shares of our Class C Preferred Stock will be subordinate to the rights of our general creditors. Shares of our Class C Preferred Stock that we issue in accordance with their terms will be fully paid and nonassessable, and will not be entitled to preemptive rights unless specified in the applicable prospectus supplement.

Our ability to issue preferred stock, or rights to purchase such shares, could discourage an unsolicited acquisition proposal. For example, we could impede a business combination by issuing a series of preferred stock containing class voting rights that would enable the holders of such preferred stock to block a business combination transaction. Alternatively, we could facilitate a business combination transaction by issuing a series of preferred stock having sufficient voting rights to provide a required percentage vote of the stockholders. Additionally, under certain circumstances, our issuance of preferred stock could adversely affect the voting power of the holders of our common stock. Although our board of directors is required to make any determination to issue any preferred stock based on its judgment as to the best interests of our stockholders, our board of directors could act in a manner that would discourage an acquisition attempt or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which stockholders might receive a premium for their stock over prevailing market prices of such stock. Our board of directors does not at present intend to seek stockholder approval prior to any issuance of currently authorized stock, unless otherwise required by law or applicable stock exchange requirements.

Terms of the Preferred Stock That We May Offer and Sell to You

We summarize below some of the provisions that will apply to the preferred stock that we may offer to you unless the applicable prospectus supplement provides otherwise. This summary may not contain all information that is important to you. You should read the prospectus supplement, which will contain additional information and which may update or change some of the information below. Prior to the issuance of a new series of preferred stock, we will further amend our third restated certificate of incorporation, as amended, designating the stock of that series and the terms of that series. We will file a copy of the certificate of designation that contains the terms of each new series of preferred stock with the SEC each time we issue a new series of preferred stock. Each certificate of designation will establish the number of shares included in a designated series and fix the designation, powers, privileges, preferences and rights of the shares of each series as well as any applicable qualifications, limitations or restrictions. You should refer to the applicable certificate of designation as well as our third restated certificate of incorporation, as amended, before deciding to buy shares of our preferred stock as described in the applicable prospectus supplement.

Our board of directors has the authority, without further action by the stockholders, to issue preferred stock in one or more series and to fix the number of shares, dividend rights, conversion rights, voting rights, redemption rights, liquidation preferences, sinking funds, and any other rights, preferences, privileges and restrictions applicable to each such series of preferred stock.

The issuance of any preferred stock could adversely affect the rights of the holders of common stock and, therefore, reduce the value of the common stock. The ability of our board of directors to issue preferred stock could discourage, delay or prevent a takeover or other corporate action.

The terms of any particular series of preferred stock will be described in the prospectus supplement relating to that particular series of preferred stock, including, where applicable:

the designation, stated value and liquidation preference of such preferred stock;

the number of shares within the series;

Table of Contents

the offering price;

the dividend rate or rates (or method of calculation), the date or dates from which dividends shall accrue, and whether such dividends shall be cumulative or noncumulative and, if cumulative, the dates from which dividends shall commence to cumulate:

whether interests in the shares of preferred stock will be represented by depositary shares as more fully described below under "Description of Depositary Shares");

any redemption or sinking fund provisions;

the amount that shares of such series shall be entitled to receive in the event of our liquidation, dissolution or winding-up;

the terms and conditions, if any, on which shares of such series shall be convertible or exchangeable for shares of our stock of any other class or classes, or other series of the same class;

the voting rights, if any, of shares of such series; the status as to reissuance or sale of shares of such series redeemed, purchased or otherwise reacquired, or surrendered to us on conversion or exchange;

the conditions and restrictions, if any, on the payment of dividends or on the making of other distributions on, or the purchase, redemption or other acquisition by us or any subsidiary, of the common stock or of any other class of our shares ranking junior to the shares of such series as to dividends or upon liquidation;

the conditions and restrictions, if any, on the creation of indebtedness by us or by any subsidiary, or on the issuance of any additional stock ranking on a parity with or prior to the shares of such series as to dividends or upon liquidation; and

any additional dividend, liquidation, redemption, sinking or retirement fund and other rights, preferences, privileges, limitations and restrictions of such preferred stock.

The description of the terms of a particular series of preferred stock in the applicable prospectus supplement will not be complete. You should refer to the applicable amendment to our third restated certificate of incorporation, as amended, for complete information regarding a series of preferred stock.

The preferred stock will, when issued against payment of the consideration payable therefor, be fully paid and nonassessable. Unless otherwise specified in the applicable prospectus supplement, each series of preferred stock will, upon issuance, rank senior to the common stock and on a parity in all respects with each other outstanding series of preferred stock. The rights of the holders of our preferred stock will be subordinate to that of our general creditors.

DESCRIPTION OF WARRANTS

We summarize below some of the provisions that will apply to the warrants unless the applicable prospectus supplement provides otherwise. This summary may not contain all information that is important to you. The complete terms of the warrants will be contained in the applicable warrant certificate and warrant agreement. These documents have been or will be included or incorporated by reference as exhibits to the registration statement of which this prospectus is a part. You should read the warrant certificate and the warrant agreement. You should also read the prospectus supplement, which will contain additional information and which may update or change some of the information below.

Table of Contents

General

We may issue, together with other securities or separately, warrants to purchase common stock, preferred stock or other securities. We may issue the warrants under warrant agreements to be entered into between us and a bank or trust company, as warrant agent, all as set forth in the applicable prospectus supplement. The warrant agent would act solely as our agent in connection with the warrants of the series being offered and would not assume any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants.

The applicable prospectus supplement will describe the following terms, where applicable, of warrants in respect of which this prospectus is being delivered:

the title of the warrants;

the designation, amount and terms of the securities for which the warrants are exercisable and the procedures and conditions relating to the exercise of such warrants;

the designation and terms of the other securities, if any, with which the warrants are to be issued and the number of warrants issued with each such security;

the price or prices at which the warrants will be issued;

the aggregate number of warrants;

any provisions for adjustment of the number or amount of securities receivable upon exercise of the warrants or the exercise price of the warrants;

the price or prices at which the securities purchasable upon exercise of the warrants may be purchased;

if applicable, the date on and after which the warrants and the securities purchasable upon exercise of the warrants will be separately transferable;

if applicable, a discussion of the material U.S. federal income tax considerations applicable to the warrants;

any other terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants;

the date on which the right to exercise the warrants shall commence and the date on which the right shall expire;

if applicable, the maximum or minimum number of warrants which may be exercised at any time;

the identity of the warrant agent;

any mandatory or optional redemption provision;

whether the warrants are to be issued in registered or bearer form;

whether the warrants are extendible and the period or periods of such extendibility;

information with respect to book-entry procedures, if any; and

any other terms of the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including the right to receive dividends, if any, or payments upon our liquidation, dissolution or winding-up or to exercise voting rights, if any.

Table of Contents

Exercise of Warrants

Each warrant will entitle the holder thereof to purchase such number of shares of common stock or preferred stock or other securities at the exercise price as will in each case be set forth in, or be determinable as set forth in, the applicable prospectus supplement. Warrants may be exercised at any time up to the close of business on the expiration date set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void. Warrants may be exercised as set forth in the applicable prospectus supplement relating to the warrants offered thereby. Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will, as soon as practicable, forward the purchased securities. If less than all of the warrants represented by the warrant certificate are exercised, a new warrant certificate will be issued for the remaining warrants.

Enforceability of Rights of Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, that holder's warrant(s).

Modification of the Warrant Agreement

The warrant agreement will permit us and the warrant agent, without the consent of the warrant holders, to supplement or amend the agreement in the following circumstances:

to cure any ambiguity;

to correct or supplement any provision which may be defective or inconsistent with any other provisions; or

to add new provisions regarding matters or questions that we and the warrant agent may deem necessary or desirable and which do not adversely affect the interests of the warrant holders.

DESCRIPTION OF DEPOSITARY SHARES

We summarize below some of the provisions that will apply to depositary shares unless the applicable prospectus supplement provides otherwise. This summary may not contain all information that is important to you. The complete terms of the depositary shares will be contained in the depositary agreement and depositary receipt applicable to any depositary shares. These documents have been or will be included or incorporated by reference as exhibits to the registration statement of which this prospectus is a part. You should read the depositary agreement and the depositary receipt. You should also read the prospectus supplement, which will contain additional information and which may update or change some of the information below.

General

We may, at our option, elect to offer fractional or multiple shares of common stock or preferred stock, rather than single shares of common stock or preferred stock (to be set forth in the prospectus supplement relating to such depositary shares). In the event we elect to do so, depositary receipts evidencing depositary shares will be issued to the public.

Table of Contents

The shares of common stock or any class or series of preferred stock represented by depositary shares will be deposited under a deposit agreement among us, a depositary selected by us, and the holders of the depositary receipts. The depositary will be a bank or trust company having its principal office in the United States and having a combined capital and surplus of at least \$50,000,000. Subject to the terms of the deposit agreement, each owner of a depositary share will be entitled, in proportion to the applicable fraction of a share of common stock or preferred stock represented by such depositary share, to all the rights and preferences of the shares of common stock or preferred stock represented by the depositary share, including dividend, voting, redemption and liquidation rights.

The depositary shares will be evidenced by depositary receipts issued pursuant to the deposit agreement. Depositary receipts will be distributed to those persons purchasing the fractional shares of common stock or the related class or series of preferred shares in accordance with the terms of the offering described in the related prospectus supplement.

DESCRIPTION OF UNITS

We may issue units comprised of one or more of the other securities described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date. The applicable prospectus supplement may describe:

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units;

the terms of the unit agreement governing the units;

United States federal income tax considerations relevant to the units; and

whether the units will be issued in fully registered global form.

This summary of certain general terms of units and any summary description of units in the applicable prospectus supplement do not purport to be complete and are qualified in their entirety by reference to all provisions of the applicable unit agreement and, if applicable, collateral arrangements and depositary arrangements relating to such units. The forms of the unit agreements and other documents relating to a particular issue of units will be filed with the SEC each time we issue units, and you should read those documents for provisions that may be important to you.

PLAN OF DISTRIBUTION

We may sell the securities covered hereby from time to time pursuant to underwritten public offerings, direct sales to the public, negotiated transactions, block trades or a combination of these methods. A distribution of the securities offered by this prospectus may also be effected through the issuance of derivative securities, including without limitation, warrants and subscriptions. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

at a fixed price or prices, which may be changed;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices;

Table of Contents

at varying prices determined at the time of sale; or

at negotiated prices.

A prospectus supplement or supplements will describe the terms of the offering of the securities, including:

the name or names of the underwriters, dealers or agents participating in the offering, if any;

the purchase price of the securities sold by us to any underwriter or dealer and the net proceeds we expect to receive from the offering;

any over-allotment options under which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts or commissions and other items constituting agents' or underwriters' compensation;

any public offering price;

any discounts or concessions allowed or reallowed or paid to dealers; and

any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. Any public offering price and any discounts or commissions or concessions allowed or reallowed or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions and other compensation we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any agents or underwriters may make a market in these securities, but will

Table of Contents

not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities. There is currently no market for any of the offered securities, other than our common stock which is listed on the NASDAQ Global Market. We have no current plans for listing of the preferred stock, warrants or subscription rights on any securities exchange or quotation system; any such listing with respect to any particular preferred stock, warrants or subscription rights will be described in the applicable prospectus supplement or other offering materials, as the case may be.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any agents and underwriters who are qualified market makers on the NASDAQ Global Market may engage in passive market making transactions in the securities on the NASDAQ Global Market in accordance with Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered hereby will be passed upon for us by Lowenstein Sandler PC, Roseland, New Jersey. If the validity of the securities offered hereby in connection with offerings made pursuant to this prospectus are passed upon by counsel for the underwriters, dealers or agents, if any, such counsel will be named in the prospectus supplement relating to such offering.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus by reference to our Annual Report on Form 10-K for the year ended December 31, 2011 have been so incorporated in reliance on the report(s) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3, including exhibits, under the Securities Act of which this prospectus forms a part. This prospectus does not contain all of the information set forth in the registration statement. This prospectus contains descriptions of certain agreements or documents that are exhibits to the registration statement. The statements as to the

Table of Contents

contents of such exhibits, however, are brief descriptions and are not necessarily complete, and each statement is qualified in all respects by reference to such agreement or document. For further information about us, please refer to the registration statement and the documents incorporated by reference in this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. The SEC's website contains reports, proxy statements and other information regarding issuers, such as Celldex Therapeutics, Inc., that file electronically with the SEC. You may also read and copy any document we file with the SEC at the SEC's Public Reference Room, located at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of its Public Reference Room. We make available free of charge through our web site our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, Proxy Statements on Schedule 14A and all amendments to those reports as soon as reasonably practicable after such material is electronically filed with or furnished to the SEC. Our website address is http://www.celldextherapeutics.com. Please note that our website address is provided as an inactive textual reference only. Information contained on or accessible through our website is not part of this prospectus or the prospectus supplement, and is therefore not incorporated by reference unless such information is otherwise specifically referenced elsewhere in this prospectus or the prospectus supplement.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" into this prospectus the information we have filed with the SEC, which means that we can disclose important information to you by referring you to those documents. Any information that we file subsequently with the SEC will automatically update this prospectus. We incorporate by reference into this prospectus the information contained in the documents listed below, which is considered to be a part of this prospectus:

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2011, filed with the SEC on March 8, 2012 (including the portions of our Proxy Statement on Schedule 14A, filed with the SEC on April 24, 2012, incorporated by reference therein);

Our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2012, June 30, 2012 and September 30, 2012, filed on May 4, 2012, August 9, 2012 and November 2, 2012, respectively;

Our Current Reports on Form 8-K filed with the SEC on February 23, 2012, February 24, 2012, March 7, 2012, April 3, 2012, June 14, 2012, September 24, 2012 and December 21, 2012 (in each case, not including any information furnished under Items 2.02 or 7.01 of Form 8-K, including the related exhibits, which information is not incorporated by reference herein);

The description of our Common Stock contained in our registration statement on Form 8-A, filed with the SEC on September 22, 1986 under Section 12 of the Securities Exchange Act, and any amendments or reports filed for the purpose of updating such description; and

The description of the rights to purchase our Series C-1 Junior Participating Cumulative Preferred Stock contained in our registration statement on Form S-4, filed with the SEC on December 21, 2007, our registration statement on Form 8-A filed with the SEC on November 8, 2004, our registration statement on Form 8-A/A filed with the SEC on October 22, 2007, our registration statement on Form 8-A/A filed with the SEC on March 7, 2008, and any amendment or report filed with the SEC for the purposes of updating such descriptions.

We also incorporate by reference all documents we file under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (a) after the initial filing date of the registration statement of which this prospectus

Table of Contents

is a part and before the effectiveness of the registration statement and (b) after the effectiveness of the registration statement and before the filing of a post-effective amendment that indicates that the securities offered by this prospectus have been sold or that deregisters the securities covered by this prospectus then remaining unsold. The most recent information that we file with the SEC automatically updates and supersedes older information. The information contained in any such filing will be deemed to be a part of this prospectus, commencing on the date on which the document is filed.

Nothing in this prospectus shall be deemed to incorporate information furnished but not filed with the SEC pursuant to Item 2.02 or 7.01 of Form 8-K.

We will furnish without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, a copy of any documents incorporated by reference other than exhibits to those documents. Requests should be addressed to:

Celldex Therapeutics, Inc.

Attention: Investor Relations 119 Fourth Avenue Needham, Massachusetts 02494 Telephone number: (781) 433-0771

Table of Contents

\$75,000,000

Common Stock

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Jefferies

Leerink Swann

February , 2013