424B5 1 d473990d424b5.htm 424B5

Table of Contents

Filed pursuant to Rule 424(b)(5)
Registration No. 333-221491

Prospectus Supplement
(To prospectus dated December 4, 2017)

5,000,000 Shares

CRISPR Therapeutics AG

Common Shares

We are offering 5,000,000 common shares to be sold in the offering.

The common shares are listed on the Nasdaq Global Market under the symbol "CRSP." The last reported sale price of the common shares on January 3, 2018 was $23.52 per share.

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

See "Risk Factors" on page S-12 of this prospectus supplement, as well as in the documents incorporated or deemed to be incorporated by reference into this prospectus supplement and the accompanying prospectus, to read more about factors you should consider before buying the common shares.

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

	Per share	Total
Public offering price	$22.750	$113,750,000
Underwriting discount(1)	$ 1.365	$ 6,825,000
Proceeds, before expenses, to CRISPR Therapeutics AG	$21.385	$106,925,000

(1) We refer you to "Underwriting" beginning on page S-57 of this prospectus supplement for additional information regarding underwriter compensation.

The underwriters have the option to purchase up to 750,000 additional common shares from us at the public offering price less the underwriting discount.

The underwriters expect to deliver the shares against payment in New York, New York on January 9, 2018.

Goldman Sachs & Co. LLC **Piper Jaffray** **Barclays**

Guggenheim Securities

Prospectus Supplement dated January 4, 2018.

Table of Contents

TABLE OF CONTENTS
PROSPECTUS SUPPLEMENT

	Page
ABOUT THIS PROSPECTUS SUPPLEMENT	S-1
WHERE YOU CAN FIND MORE INFORMATION	S-2
INCORPORATION BY REFERENCE	S-2
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS	S-3
PROSPECTUS SUPPLEMENT SUMMARY	S-5
THE OFFERING	S-10
RISK FACTORS	S-12
USE OF PROCEEDS	S-52
DILUTION	S-53
PRICE RANGE OF COMMON SHARES	S-55
DIVIDEND POLICY	S-56
UNDERWRITING	S-57
MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS	S-64
LEGAL MATTERS	S-69
EXPERTS	S-69

PROSPECTUS

ABOUT THIS PROSPECTUS	1
CRISPR THERAPEUTICS AG	2
RISK FACTORS	3
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	4
RATIO OF EARNINGS TO FIXED CHARGES	5
USE OF PROCEEDS	6
COMPARISON OF SWISS LAW AND DELAWARE LAW	11
DESCRIPTION OF DEBT SECURITIES	18
DESCRIPTION OF WARRANTS	24
DESCRIPTION OF UNITS	25
DESCRIPTION OF SUBSCRIPTION RIGHTS	28
PLAN OF DISTRIBUTION	29
LEGAL MATTERS	31
EXPERTS	31
WHERE YOU CAN FIND MORE INFORMATION	31
INCORPORATION OF CERTAIN INFORMATION BY REFERENCE	31

We have not authorized anyone to provide any information or to make any representations other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus we have prepared. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement and the accompanying prospectus is current only as of its date.

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of the registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process and consists of two parts. The first part is this prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, gives more general information, some of which may not apply to this offering. Generally, when we refer to the "prospectus," we are referring to both parts combined. This prospectus supplement may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with the accompanying prospectus or with any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference into each include important information about us, the securities being offered and other information you should know before investing in our securities. You should also read and consider information in the documents we have referred you to in the sections of this prospectus supplement entitled "Where You Can Find More Information" and "Incorporation by Reference" and the accompanying prospectus entitled "Where You Can Find More Information" and "Incorporation by Reference."

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We take no responsibility for, and can provide no assurances as to the reliability of, any information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We are not offering to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate as of any date other than as of the date of this prospectus supplement or the accompanying prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our securities. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

Unless otherwise stated, all references in this prospectus supplement or the accompanying prospectus to "us," "our," "CRISPR," "CRISPR Therapeutics AG," "we," the "Company" and similar designations refer, collectively, to CRISPR Therapeutics AG, a Swiss stock corporation (*Aktiengesellschaft*), and its consolidated subsidiaries, CRISPR Therapeutics, Inc. and CRISPR Therapeutics Ltd.

No action is being taken in any jurisdiction outside the United States to permit a public offering of the securities or possession or distribution of this prospectus supplement or the accompanying prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement or the accompanying prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement or the accompanying prospectus applicable to that jurisdiction.

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

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 *www.sec.gov*. Copies of certain information filed by us with the SEC are also available on our website at *www.crisprtx.com*. Our website is not a part of this prospectus supplement or the accompanying prospectus and is not incorporated by reference in this prospectus supplement or the accompanying prospectus. You may also read and copy any document we file at the SEC's Public Reference Room, 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 the Public Reference Room.

This prospectus supplement is part of a registration statement we filed with the SEC. This prospectus supplement, filed as part of the registration statement, omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus supplement concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's website.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement and the accompanying prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement, the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement incorporates by reference the documents listed below (File No. 001-37923) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of this prospectus supplement and the termination of this offering:

- Annual Report on Form 10-K for the fiscal year ended December 31, 2016, which was filed with the SEC on March 10, 2017, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement (other than information furnished rather than filed) for the 2017 Annual General Meeting of Shareholders, which was filed with the SEC on April 18, 2017;
- Quarterly Report on Form 10-Q for the fiscal quarters ended March 31, 2017, June 30, 2017 and September 30, 2017; which were filed with the SEC on May 11, 2017, August 10, 2017 and November 8, 2017, respectively;
- Current Reports on Form 8-K filed with the SEC on February 15, 2017, March 20, 2017, March 31, 2017, April 13, 2017, April 27, 2017, May 4, 2017, June 2, 2017, June 8, 2017, June 19, 2017, July 25, 2017, July 27, 2017, October 2, 2017, November 7, 2017, November 13, 2017, December 7, 2017, December 18, 2017 and December 21, 2017.
- The description of our common shares contained in our Registration Statement on Form 8-A filed with the SEC on October 18, 2016, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by contacting us, either orally or in writing, at the following:

CRISPR Therapeutics AG
Baarerstrasse 14
6300 Zug

Switzerland
Attn: Investor Relations
ir@crisprtx.com
Phone: 339-970-2843

S-2

Table of Contents

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein contain statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. All statements, other than statements of historical facts, contained or incorporated by reference in this prospectus are forward-looking statements. In some cases, you can identify forward-looking statements by words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "seek," "should," "target," "will," "would" or the negative of these words or other comparable terminology, although not all forward-looking statements contain these identifying words. Forward-looking statements include, but are not limited to, statements about:

- the initiation, cost, timing, progress and results of our research and development activities, preclinical studies and future clinical trials;
- our ability to create a pipeline of product candidates;
- our ability to advance any product candidate into, and successfully complete clinical trials;
- our ability to obtain and maintain regulatory approval of our future product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- our plans to research, develop and commercialize our future product candidates;
- the success of our joint venture with Bayer HealthCare LLC and our collaboration with Vertex Pharmaceuticals, Incorporated;
- our ability to obtain and maintain intellectual property protection for our future product candidates;
- the size and growth potential of the markets for our future product candidates, and our ability to serve those markets;
- our ability to successfully commercialize our current and future product candidates;
- the rate and degree of market acceptance of our current and future product candidates;
- regulatory developments in the United States and foreign countries;
- developments relating to gene-editing technologies including CRISPR/Cas9;
- the success of competing therapies that are or become available;
- our ability to retain key scientific or management personnel;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our use of the proceeds from this offering; and
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and need for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important

Table of Contents

factors in the cautionary statements included in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, particularly in the "Risk factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or enter into.

You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, as well as the documents that we have filed as exhibits to the registration statement of which this prospectus supplement forms a part, completely and with the understanding that our actual future results, performance or achievements may be materially different from what we expect. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein contains industry, market and competitive position data that are based on industry publications and studies conducted by third parties as well as our own internal estimates and research. These industry publications and third-party studies generally state that the information that they contain has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We are responsible for all of the disclosure contained in this prospectus, and we believe these industry publications and third-party research, surveys and studies are reliable.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents incorporated by reference herein or therein. This summary does not contain all the information that you should consider before investing in our common shares. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the risks of investing in our common shares discussed under "Risk Factors" beginning on page S-12 of this prospectus supplement, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision. This prospectus supplement may add to, update or change information in the accompanying prospectus.

Our Business

Overview

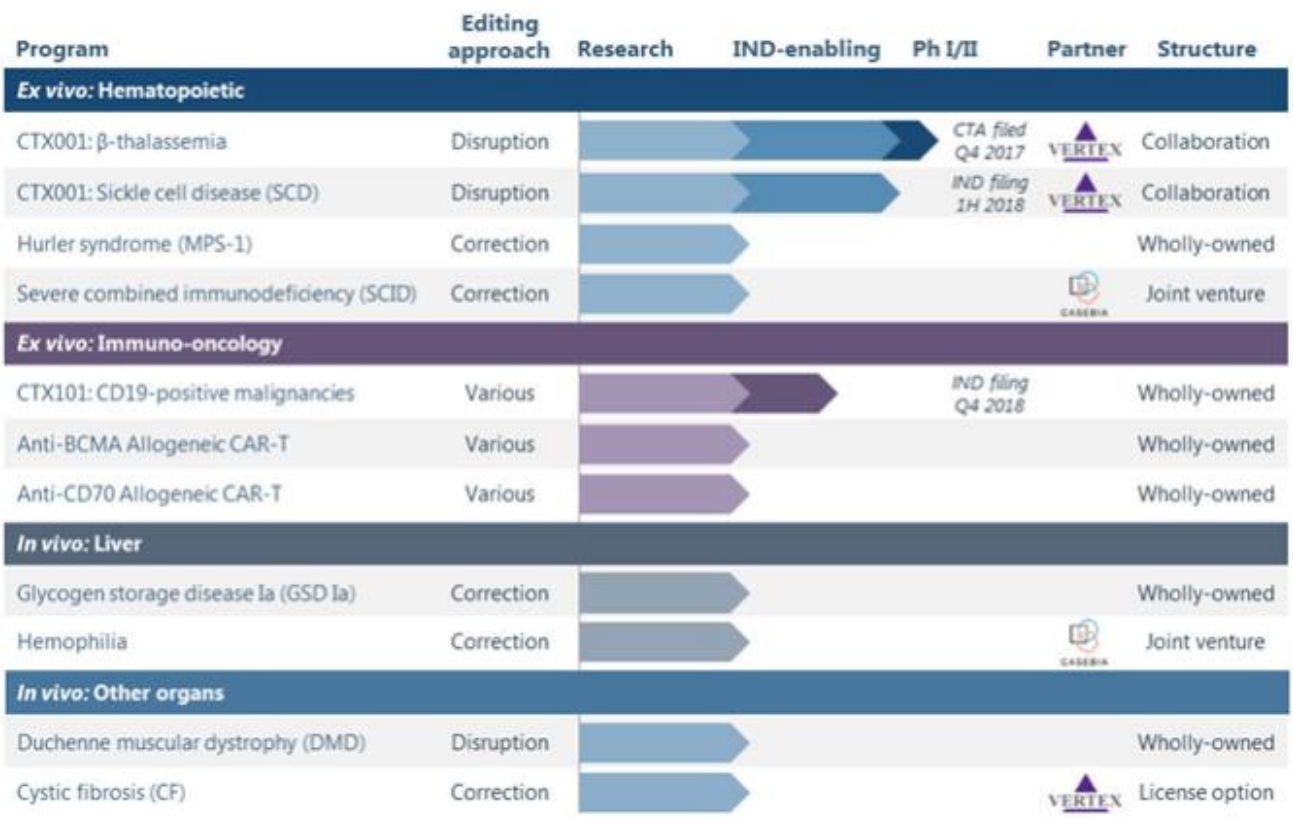
We are a leading gene editing company focused on the development of CRISPR/Cas9-based therapeutics. CRISPR/Cas9 stands for Clustered, Regularly Interspaced Short Palindromic Repeats (CRISPR) Associated protein-9 and is a revolutionary technology for gene editing, the process of precisely altering specific sequences of genomic DNA. We are applying this technology to potentially treat a broad set of both rare and common diseases by disrupting, correcting or regulating disease-related genes. We believe that our scientific expertise, together with our gene editing approach, may enable an entirely new class of highly effective and potentially curative treatments for patients for whom current biopharmaceutical approaches have had limited success. Our most advanced programs target beta-thalassemia and sickle cell disease, two hemoglobinopathies that have high unmet medical need.

We are pursuing a two-pronged product development strategy using both *ex vivo* and *in vivo* approaches. Our most advanced programs in hemoglobinopathies, which we refer to as CTX001, use an *ex vivo* approach, whereby cells are harvested from a patient, treated with a CRISPR/Cas9-based therapeutic and reintroduced into the patient. In December 2017, we entered into a joint development and commercialization agreement with Vertex Pharmaceuticals, Inc., or Vertex, for the development and commercialization of CTX001 (see "—Recent Developments"). Beyond these lead programs, we are pursuing a number of additional *ex vivo* applications, as well as select *in vivo* applications whereby the CRISPR/Cas9 therapeutic is delivered directly to target cells within the human body. Our initial *in vivo* applications will leverage well-established delivery technologies for gene-based therapeutics.

Our Pipeline

We have established a portfolio of programs by selecting disease targets based on a number of criteria, including high unmet medical need, advantages of CRISPR/Cas9 relative to alternative approaches, technical feasibility and the time required to advance the product candidate into and through clinical trials. We have initiated programs in four primary areas: (i) *ex vivo* programs involving gene editing of hematopoietic cells, (ii) *ex vivo* programs targeting CD-19 positive malignancies, (iii) *in vivo* programs targeting the liver and (iv) additional *in vivo* programs targeting other organ systems, such as muscle and lung. The following table summarizes the current status of our product development pipeline:

Table of Contents



Ex Vivo *Hematopoietic Programs*

We are primarily utilizing *ex vivo* approaches to treat diseases related to the hematopoietic system, which is the system of organs and tissues, such as bone marrow, the spleen and lymph nodes, involved in the production of blood. When a suitable donor can be found, many of the hematopoietic system diseases we are targeting are treated with allogeneic hematopoietic stem cell transplants, or allo-HSCT. Patients who undergo allo-HSCT face a high risk of complications such as infections related to immunosuppression, transplant rejection and graft-versus-host disease.

Our Lead Programs—Hemoglobinopathies

Hemoglobinopathies are a diverse group of inherited blood disorders that result from variations in the synthesis or structure of hemoglobin. Our lead programs in hemoglobinopathies, for which we have partnered with Vertex, aim to develop a single, potentially transformative CRISPR/Cas9-based therapy to treat both beta-thalassemia and sickle cell disease, or SCD. These diseases are caused by mutations in the gene encoding the beta globin protein. A number of factors make these attractive lead indications, including: (i) high unmet medical need, (ii) compelling market potential, (iii) well understood genetics and (iv) the ability to employ an *ex vivo* gene disruption strategy.

Beta-thalassemia is caused by mutations that give rise to insufficient expression of the beta globin protein, resulting in anemia requiring regular blood transfusions. SCD is an inherited disorder caused by a mutation in the beta globin gene resulting in abnormal red blood cells, which obstruct blood vessels, resulting in a variety of severe symptoms and early mortality. The total worldwide annual incidence of beta-thalassemia and SCD is estimated to be 60,000 and 300,000 births, respectively.

Our therapeutic approach to treat these diseases employs gene editing technology to upregulate the expression of fetal hemoglobin, or HbF, a form of hemoglobin that is present in newborn infants and is replaced by adult hemoglobin. Studies have shown that patients with beta-thalassemia and sickle cell disease who maintain elevated levels

HbF are asymptomatic or may have mild disease symptoms. In preclinical studies, our CRISPR gene editing process demonstrated the ability to edit cells with approximately 80% efficiency in a bulk population of cells, which resulted in greater than 30% HbF expression, compared to approximately 10% HbF expression in the control arm of the study. On a per cell basis, more than 90% of cells had modifications at the desired location, with 76% of the cells having edits made on both copies of the target gene, and 16% of the cells having edits made on one copy of the target gene. We estimate that this editing rate results in HbF expression levels of greater than 35% in the cells that had edits on both copies of the target gene, and over 20% for cells edited at one gene. In other preclinical mouse models, the gene-edited cells also maintained the ability to engraft long-term in a mouse model. We believe our *ex vivo* gene editing approach, utilizing the patient's own cells, has the potential to provide better safety and efficacy profiles than currently available treatments.

Table of Contents

In December 2017, we submitted clinical trial applications in various European jurisdictions for CTX001 in beta-thalassemia and we expect to file an investigational new drug application with the United States Food and Drug Administration for CTX001 targeting SCD in the first half of 2018. We have designed a single arm Phase 1/2 study in which we plan to enroll up to 30 adult patients to assess the safety and efficacy of CTX001 in patients with beta-thalassemia.

Other Hematopoietic Programs

There are numerous additional diseases that are potentially treatable through *ex vivo* gene editing of the hematopoietic system. We plan to apply the capabilities we are developing in hemoglobinopathies to treat other diseases. We have launched programs in two such diseases, severe combined immunodeficiency disease, or SCID, and Hurler syndrome, a genetic metabolic disorder. In addition, we are utilizing our *ex vivo* gene editing expertise to advance our efforts in cell therapies for immuno-oncology applications.

In Vivo *Programs*

We are pursuing a number of *in vivo* indications in parallel with our *ex vivo* programs, which will involve delivery of CRISPR/Cas9 therapeutics directly to target tissues within the human body. Our initial *in vivo* applications will target the liver, leveraging well-established delivery technologies. We intend to customize and use these delivery technologies for programs in hemophilia and genetic diseases of liver metabolism, including Glycogen Storage Disease Ia.

We intend to optimize delivery technologies to target select *in vivo* indications outside the liver such as Duchenne muscular dystrophy and cystic fibrosis. We believe that our CRISPR/Cas9 gene editing technology is well suited to address these diseases, both of which have significant patient populations with high unmet medical need. We are working internally, as well as through third-party collaborations, to optimize viral and non-viral delivery technologies for use in these diseases. We have observed promising preclinical results in our studies with both viral and non-viral delivery technologies. Using non-viral delivery technology such as lipid nanoparticles, we were able to demonstrate approximately 80% editing rates in mouse models at the target gene which resulted in greater than 85% reduction in the expression of the gene as measured by protein levels in the serum.

Engineered Cell Therapies in Immuno-oncology

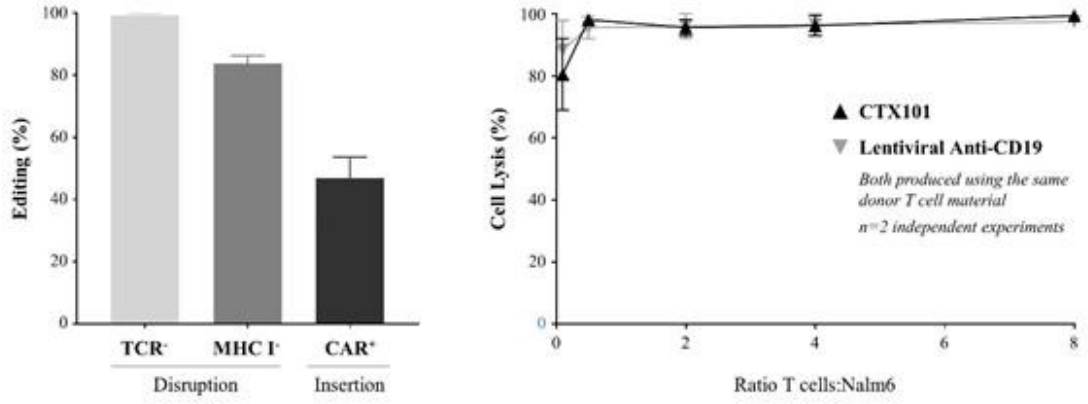
Over the past several years, interest in the oncology community has grown rapidly in the field of immuno-oncology, or treatments that harness the immune system to attack cancer cells. Engineered cell therapy is one such immunotherapy approach, in which immune system cells such as T-cells are genetically modified to enable them to recognize and attack cancer cells.

Engineered cell therapy has demonstrated encouraging results leading to two recent approvals for autologous CD-19 chimeric antigen receptor T-cell, or CAR-T, products, and may become an entirely new class of oncology therapeutics; however, realizing this full potential will require overcoming some key challenges. Most engineered cell therapies in development require unique products to be created for each patient treated, using conventional techniques, making this approach to drug development often inefficient and cost prohibitive. Additionally, these versions of engineered cell therapies appear limited in their ability to treat solid tumors and have demonstrated sub-optimal safety profiles, including the occurrence of cytokine release syndrome, an overstimulation of the immune system, which can result in death.

We expect that the cellular engineering strategies that are ultimately successful in immuno-oncology will involve multiple genetic modifications, an application for which we believe CRISPR/Cas9 will play a central role. While other gene editing platforms could potentially be used for these purposes, CRISPR/Cas9 is particularly well-suited for multiplexed editing, which is the modification of multiple genes within a single cell. Current gene editing techniques that require different protein enzymes for each genetic modification may be limited in the number of edits they can make concurrently due to efficiency, cytotoxicity, and/or manufacturing challenges. In contrast, CRISPR/Cas9 has the potential to efficiently make multiple edits using a single Cas9 protein and multiple small guide RNA molecules.

Our lead immuno-oncology product candidate, CTX101, is a healthy-donor derived allogeneic CAR-T cell targeting CD-19 positive malignancies. A primary aim of CTX101 is to overcome the inefficiency and cost of creating a unique product for each patient in a tumor type by treating many different patients from a single batch, which we refer to as being an "off-the-shelf" therapy. In order to generate CTX101, we make three modifications to T-cells taken from healthy donors using our CRISPR/Cas9 technology: (i) the T cell receptor, or TCR, is eliminated to reduce the risk of graft versus host disease from the product, (ii) a CD-19 directed CAR is inserted site-specifically into the TCR gene and (iii) the class I major histocompatibility complex, MHCI, is removed from the cell surface in order to improve the persistence of the CAR-T cells in an "off-the-shelf" setting. We believe this approach will have advantages over other allogeneic CAR-T products in development that semi-randomly insert the CAR using an integrating virus, and do not include the MHCI knockout to increase persistence. As shown in the figure below, we have demonstrated the ability to perform the edits necessary to generate CTX101 at high efficiency, and that in preclinical testing CTX101 has comparable cytotoxic activity to currently approved CD-19 CAR-T products. We have transferred production of CTX101 to a GMP-capable CMO, and intend to file an IND for CTX101 by the end of 2018.

Table of Contents



Other Immuno-oncology Programs

Beyond CTX101, we are developing additional CAR-T programs directed to other tumor targets including B-cell maturation antigen, or BCMA, and CD-70. These programs will leverage many of the capabilities and reagents developed for CTX101, potentially enabling them to progress quickly into development. We have observed promising anti-tumor activity in our preclinical studies directed to CD-70, where our product candidate eradicated tumors in a mouse model for renal cell carcinoma. In these future programs, we may use the multiplexing ability of CRISPR/Cas9 to introduce additional genetic edits, such as the removal of checkpoint inhibitors or introduction of safety elements, in order to improve the efficacy and safety profile of these products and potentially realize the full potential of engineered cell therapy in immuno-oncology across many tumor types including sold tumors.

Recent Developments

On December 12, 2017, we, along with CRISPR Therapeutics, Inc., CRISPR Therapeutics Limited and TRACR Hematology Ltd, entered into a Joint Development and Commercialization Agreement, or the JDA, with Vertex and Vertex Pharmaceuticals (Europe) Limited, together referred to as Vertex. The initial focus of the JDA is for the development of CTX001 for beta-thalassemia and SCD. In connection with entering into the JDA, we received a $7.0 million up-front payment from Vertex and are eligible for a one-time low seven digit milestone payment upon the dosing of the second patient in a clinical trial with the initial product candidate. The net profits and net losses, as applicable, incurred under the JDA will be shared equally between us and Vertex.

Table of Contents

Implications of Being an Emerging Growth Company

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earlier of (i) December 31, 2021; (ii) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, which means the market value of our common shares that are held by non-affiliates exceeds $700 million as of June 30th of the previous year. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies.

Company Information

We were incorporated as a Swiss stock corporation *(Aktiengesellschaft)* on October 28, 2013 under the name Inception Genomics AG. We changed our name to CRISPR Therapeutics AG on April 28, 2014. Our principal executive offices are located at Baarerstrasse 14, 6300 Zug, Switzerland and our telephone number is + 41 41 561 32 77. Our website is *www.crisprtx.com*. Our website and the information contained therein or connected thereto are not incorporated into this prospectus supplement, the accompanying prospectus or the registration statement of which they form part.

The trademarks, trade names and services marks appearing in this prospectus supplement and the accompanying prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Table of Contents

THE OFFERING

Common shares offered by us	5,000,000 shares
Common shares outstanding following the offering	45,890,954 shares (or 46,640,954 shares if the underwriters exercise their option to purchase additional shares in full)
Underwriters' option to purchase additional shares	We have granted the underwriters an option to purchase up to an additional 750,000 shares. The underwriters can exercise this option at any time within 30 days from the date of this prospectus supplement.
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $106.6 million (or approximately $122.6 million if the underwriters exercise their option to purchase additional shares in full) after deducting estimated underwriting discounts and estimated offering expenses. We intend to use the net proceeds from this offering to fund clinical development of CTX001, CTX101 and additional pipeline candidates, platform extensions, and manufacturing, working capital and general corporate purposes. See "Use of Proceeds" for additional information.
Subscription Rights Offering	Pursuant to the Swiss Code of Obligations, subject to limited exceptions, shareholders have statutory pre-emptive rights to subscribe for new shares on a pro-rata basis (measured by their existing shareholdings) in connection with new issuances of shares. With respect to conditional capital in connection with the issuance of conversion rights, convertible bonds or similar debt instruments, shareholders have, subject to limited exceptions, statutory advance subscription rights for the subscription of conversion rights, convertible bonds or similar debt instruments. The common aim of such pre-emptive rights and advance subscription rights is to provide existing shareholders with statutory legal means against dilution in the case of a capital increase. In connection with this offering, our board of directors resolved that it was in the best interests of our shareholders to exclude their pre-emptive rights in this offering in order to facilitate a "fast and flexible" public offering which likely could not be effected without the exclusion of the statutory pre-emptive right of our existing shareholders. Based on the public offering price in this offering and the discount it represents to the closing price of our common shares on January 4, 2018, our board of directors has determined that we will not need to grant our shareholders subscription rights after the conclusion of this offering, to allow them to purchase their pro rata portion of shares as if they had participated in this offering.
Risk factors	Investing in our common shares involves risks. See "Risk Factors" beginning on page S-12 of this prospectus supplement and other information included or incorporated by reference into this prospectus supplement and the accompanying prospectus for a discussion of the factors you should carefully consider before deciding to invest in our securities.
The Nasdaq Global Market symbol	"CRSP"

The number of common shares to be outstanding after the offering is based on 40,890,954 common shares outstanding as of September 30, 2017, including 64,227 issued but unvested restricted shares, but excludes:

- 5,778,629 of our common shares issuable upon the exercise of options outstanding under our 2015 Stock Option and Grant Plan, or the 2015 Stock Option Plan, as of September 30, 2017 at a weighted-average exercise price of $12.36 per common share;

Table of Contents

- 5,468,024 of our common shares reserved for future issuance under our Amended and Restated 2016 Stock Option and Incentive Plan, or the Amended and Restated 2016 Stock Option Plan, plus any future increases in the number of common shares reserved for issuance under the Amended and Restated 2016 Stock Option Plan pursuant to the evergreen provision of the Amended and Restated 2016 Stock Option Plan; and
- 413,226 common shares reserved for issuance under our 2016 Employee Stock Purchase Plan, or ESPP.

Except as otherwise indicated, all information in this prospectus supplement assumes:

- no exercise of stock options after September 30, 2017; and
- no exercise of the underwriters' option to purchase additional common shares in this offering.

Table of Contents

RISK FACTORS

Investing in our common shares involves significant risks. In addition to the other information contained in this prospectus supplement, the accompanying prospectus and in the documents that we have incorporated by reference, you should carefully consider the risks discussed below, before making a decision about investing in our common shares. Such risks and uncertainties and those discussed below are not the only ones facing us. Additional risks and uncertainties not presently known to us, or that we currently see as immaterial, may also harm our business. If any of these risks occur, our business, financial condition and operating results could be harmed, the trading price of our common shares could decline and you could lose part or all of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We Have Incurred Significant Operating Losses Since Our Inception And Anticipate That We Will Incur Continued Losses For The Foreseeable Future.

We have funded our operations to date through proceeds from our initial public offering, or the IPO, and concurrent private placement of our common shares, private placements of our preferred shares and convertible securities and payments received from Casebia Therapeutics, LLC pursuant to our joint venture with Bayer HealthCare LLC, or Bayer Healthcare, and our collaboration with Vertex Pharmaceuticals, Incorporated, or Vertex. Since inception, we have incurred significant operating losses. Our net loss was $23.2 million, $25.8 million, and $6.8 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016 and 2015, we had an accumulated deficit of $57.1 million and $33.9 million, respectively. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our shareholders' deficit and working capital. We anticipate that our expenses will increase substantially if and as we:

- continue our current research programs and our preclinical and clinical development of product candidates, including our lead hemoglobinopathy program, CTX001, targeting beta-thalassemia and sickle cell disease and our lead immuno-oncology product candidate, CTX101;
- seek to identify additional research programs and additional product candidates;
- conduct Investigational New Drug, or IND, supporting preclinical studies and initiate clinical trials for our most advanced product candidates which are from our hemoglobinopathy program targeting beta-thaleassemia and sickle cell disease;
- initiate preclinical studies and clinical trials for any other product candidates we identify and choose to develop;
- maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials;
- further develop our gene editing technology;
- hire additional clinical, quality control and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product candidate development;
- acquire or in-license other technologies;
- ultimately establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval; and
- operate as a public company.

As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing gene editing product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

We Will Need To Raise Substantial Additional Funding, Which Will Dilute Our Shareholders. If We Are Unable To Raise Capital When Needed, We Would Be Forced To Delay, Reduce Or Eliminate Some Of Our Product Development Programs Or Commercialization Efforts.

Table of Contents

The development of gene editing product candidates is capital intensive. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate preclinical studies and clinical trials for and seek marketing approval for our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of Bayer Healthcare or Vertex, or other future collaborators. We may also need to raise additional funds sooner if we choose to pursue additional indications or geographies for our product candidates or otherwise expand more rapidly than we presently anticipate. In addition, relative to prior years when we were a private company, we expect to incur significant additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our research and development programs or future commercialization efforts.

As of December 31, 2016 and September 30, 2017, we had cash of approximately $315.5 million and $253.5 million, respectively. We expect that our cash balance at September 30, 2017 will enable us to fund our operating expenses and capital expenditure requirements for at least the next 24 months.

Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our wholly-owned and partnered product candidates;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of establishing and maintaining a supply chain for the development and manufacture of our product candidates;
- the success of our current joint venture with Bayer Healthcare and our collaboration with Vertex;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the costs of fulfilling our obligations under the Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement to reimburse other parties for costs incurred in connection with the prosecution and maintenance of associated patent rights;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of establishing or contracting for manufacturing capabilities if we obtain regulatory approvals to manufacture our product candidates;
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our product candidates; and
- our ability to establish and maintain healthcare coverage and adequate reimbursement.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible

securities would dilute all of our shareholders and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions

Table of Contents

that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

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

We Have A Limited Operating History, Which May Make It Difficult To Evaluate Our Technology And Product Development Capabilities And Predict Our Future Performance.

We are early in our development efforts and we have not initiated clinical trials for any of our product candidates. We were formed in October 2013, have no products approved for commercial sale and have not generated any revenue from product sales. Our ability to generate product revenue or profits, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We may never be able to develop or commercialize a marketable product.

We have submitted clinical trial applications, or CTAs, in various European jurisdictions for a clinical trial in beta-thalassemia for our lead product candidate from our hemoglobinopathy program and intend to file an IND with the United Stated Food and Drug Administration, or FDA for our hemoglobinopathy program targeting sickle cell disease in the first half of 2018, but have not yet commenced clinical trials for such programs. Each of our other programs requires additional discovery research and then preclinical development. All of our programs, including our hemoglobinopathy program, require clinical development, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. In addition, our product candidates must be approved for marketing by the FDA or certain other health regulatory agencies, including the European Medicines Agency, or EMA, before we may commercialize any product.

Our limited operating history, particularly in light of the rapidly evolving gene editing field, may make it difficult to evaluate our technology and industry and predict our future performance. Our short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer. Similarly, we expect that our financial condition and operating results will fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. As a result, our shareholders should not rely upon the results of any quarterly or annual period as an indicator of future operating performance.

In addition, as an early stage company, we have encountered unforeseen expenses, difficulties, complications, delays and other known and unknown circumstances. As we advance our product candidates, we will need to transition from a company with a research focus to a company capable of supporting clinical development and if successful, commercial activities. We may not be successful in such a transition.

Our Ability To Use Tax Loss Carryforwards In Switzerland May Be Limited.

Under Swiss law, we are entitled to carry forward losses we incur for a period of seven years and we can offset future profits, if any, against such losses. As of December 31, 2016, we reported tax loss carry forwards from inception through 2015 for purposes of Swiss federal direct taxes in the aggregate amount of CHF 22.0 million. Due to the accepted mixed company status (the tax ruling with respect to the mixed company status was accepted in February 2017 with retroactive effect as from 2013/2014) the tax losses available to offset future income at cantonal level amount to CHF 4.1 million. If not used, these tax losses will expire seven years after the year in which they occurred. Due to our limited income, there is a high risk that the tax loss carry forwards will expire partly or entirely. For 2016, the tax return has – in accordance with Swiss tax law – not yet been filed. Therefore, for 2016 the loss carried forward will only be claimed with filing of the tax return for the tax year 2016.

Risks Related to Our Business, Technology and Industry

We Are Early In Our Development Efforts And We Have Not Initiated Clinical Trials For Any Of Our Product Candidates. It Will Be Many Years Before We Or Our Collaborators Commercialize A Product Candidate, If Ever. If We Are Unable To Advance Our Product Candidates To Clinical Development, Obtain Regulatory Approval And Ultimately Commercialize Our Product Candidates, Or Experience Significant Delays In Doing So, Our Business Will Be Materially Harmed.

Table of Contents

We are early in our development efforts and have focused our research and development efforts to date CRISPR/Cas9, gene editing technology, identifying our initial targeted disease indications and our initial product candidates. Our future success depends heavily on the successful development of our CRISPR/Cas9 gene editing product candidates including our most advanced product candidate, CTX001, which targets beta-thalassemia and sickle cell disease. We have invested substantially all of our efforts and financial resources in the identification and preclinical development of our current product candidates. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. For example, our research programs, including those subject to our joint venture with Bayer Healthcare and collaboration agreement and the Joint Development and Commercialization Agreement, or the JDA, with Vertex, may fail to identify potential product candidates for clinical development for a number of reasons or may fail to successfully advance any product candidates through clinical development. Our research methodology may be unsuccessful in identifying potential product candidates, or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products impractical to manufacture, unmarketable, or unlikely to receive marketing approval. We currently generate no revenue from sales of any product and we may never be able to develop or commercialize a marketable product.

In December 2017, we submitted CTAs in various European jurisdictions for CTX001 to begin our first clinical trial in beta-thalassemia and plan, following a pre-IND meeting with the FDA, to file an IND with the FDA in the first half of 2018 to begin our first clinical trial for CTX001 in sickle cell disease. The filing of future CTAs or INDs for any other product candidate we develop is subject to the identification and selection of guide RNA with acceptable efficiency and the successful completion of preclinical toxicology testing. Commencing any of our clinical trials is also subject to acceptance by the European regulatory authorities of our CTAs, or the FDA of our INDs, and finalizing the trial design based on discussions with the applicable regulatory authorities, including the Recombinant DNA Advisory Committee, or RAC, of the U.S. National Institutes of Health, or NIH. In the event that the European regulatory authorities, FDA or RAC requires us to complete additional preclinical studies or we are required to satisfy other requests, the start of our first clinical trial for our hemoglobinopathy programs or any of our other programs may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, they could disagree that we have satisfied their requirements to commence our clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect.

Our product candidates will require additional preclinical and clinical development, regulatory and marketing approval in multiple jurisdictions, obtaining manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. In addition, our product development programs must be approved for marketing by the FDA, EMA or certain other health regulatory agencies, before we may commercialize our product candidates.

The success of our product candidates will depend on several factors, including the following:

- successful completion of preclinical studies;
- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- ability to develop safe and effective delivery mechanisms for our *in vivo* therapeutic programs;
- ability to identify optimal RNA sequences to guide genomic editing;
- entry into collaborations to further the development of our product candidates;
- a positive recommendation of the Recombinant DNA Advisory Committee of the NIH;
- approval of CTAs or INDs for our product candidates to commence clinical trials;
- successful enrollment in, and completion of, preclinical studies and clinical trials;
- successful data from our clinical program that supports an acceptable risk-benefit profile of our product candidates for the intended patient populations;
- receipt of regulatory and marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers for clinical supply and commercial manufacturing and, where applicable, commercial manufacturing capabilities;

Table of Contents

- successful development of our internal manufacturing processes and transfer to larger-scale facilities operated by either a contract manufacturing organization, or CMO, or by us;
- establishment and maintenance of patent and trade secret protection or regulatory exclusivity for our product candidates;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors;
- effective competition with other therapies and treatment options;
- establishment and maintenance of healthcare coverage and adequate reimbursement;
- enforcement and defense of intellectual property rights and claims;
- maintenance of a continued acceptable safety profile of the product candidates following approval; and
- achieving desirable medicinal properties for the intended indications.

Additionally, because our technology involves gene editing across multiple cell and tissue types, we are subject to many of the challenges and risks that gene therapies face, including:

- regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future; to date, no products that involve the genetic modification of patient cells have been approved in the United States and only one gene therapy product has been approved in the European Union;
- improper insertion of a gene sequence into a patient's chromosome could lead to lymphoma, leukemia or other cancers, or other aberrantly functioning cells; and
- the FDA recommends a follow-up observation period of 15 years or longer for all patients who receive treatment using gene therapies, and we may need to adopt and support such an observation period for our product candidates.

If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

Our CRISPR/Cas9 Gene Editing Product Candidates Are Based On A New Gene Editing Technology, Which Makes It Difficult To Predict The Time And Cost Of Development And Of Subsequently Obtaining Regulatory Approval, If At All. There Have Only Been A Limited Number Of Clinical Trials Of Product Candidates Based On Gene Editing Technology And No Gene Editing Products Have Been Approved In The United States Or In The European Union.

CRISPR/Cas9 gene editing technology is relatively new and no products based on CRISPR/Cas9 or other similar gene editing technologies have been approved in the United States or the European Union and only a limited number of clinical trials of products based on gene editing technologies have been commenced. As such it is difficult to accurately predict the developmental challenges we may incur for our product candidates as they proceed through product discovery or identification, preclinical studies and clinical trials. In addition, because we have not commenced clinical trials, we have not yet been able to assess safety in humans, and there may be long-term effects from treatment with any product candidates that we develop that we cannot predict at this time. Any product candidates we may develop will act at the level of DNA, and, because animal DNA differs from human DNA, testing of our product candidates in animal models may not be predictive of the results we observe in human clinical trials of our product candidates for either safety or efficacy. Also, animal models may not exist for some of the diseases we choose to pursue in our programs. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our gene editing technology, or any similar or competitive gene editing technologies, will result in the identification, development, and regulatory approval of any products. There can be no assurance that any development problems we experience in the future related to our gene editing technology or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

Table of Contents

The clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. No products based on gene editing technologies have been approved by regulators. As a result, the regulatory approval process for product candidates such as ours is uncertain and may be more expensive and take longer than the approval process for product candidates based on other, better known or more extensively studied technologies. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or the European Union or how long it will take to commercialize our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product candidate to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects may be harmed.

The FDA, The NIH And The EMA Have Demonstrated Caution In Their Regulation Of Gene Therapy Treatments, And Ethical And Legal Concerns About Gene Therapy And Genetic Testing May Result In Additional Regulations Or Restrictions On The Development And Commercialization Of Our Product Candidates, Which May Be Difficult To Predict.

The FDA, NIH and the EMA have each expressed interest in further regulating biotechnology, including gene therapy and genetic testing. For example, the EMA advocates a risk-based approach to the development of a gene therapy product. Agencies at both the federal and state level in the United States, as well as the U.S. congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some or all of our product candidates. Within the broader genome product field, uniQure N.V.'s Glybera has received marketing authorization from the European Commission, and to date no gene therapy products have received marketing approval in the United States.

Regulatory requirements in the United States and in other jurisdictions governing gene therapy products have changed frequently and may continue to change in the future. The FDA established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research to consolidate the review of gene therapy and related products, and established the Cellular, Tissue and Gene Therapies Advisory Committee to advise this review. Prior to submitting an IND, our human clinical trials are subject to review by the NIH Office of Biotechnology Activities, or OBA, Recombinant DNA Advisory Committee, or the RAC. Following an initial review, RAC members make a recommendation as to whether the protocol raises important scientific, safety, medical, ethical or social issues that warrant in-depth discussion at the RAC's quarterly meetings. Even though the FDA decides whether individual gene therapy protocols may proceed under an IND, the RAC's recommendations are shared with the FDA and the RAC public review process, if undertaken, can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and has not objected to its initiation or has notified the sponsor that the study may begin. Conversely, the FDA can put an IND on a clinical hold even if the RAC has provided a favorable review or has recommended against an in-depth, public review. Moreover, under guidelines published by the NIH, patient enrollment in our future gene editing clinical trials cannot begin until the investigator for such clinical trial has received a letter from the OBA indicating that the RAC review process has been completed; and Institutional Biosafety Committee, or IBC, approval as well as all other applicable regulatory authorizations have been obtained. In addition to the government regulators, the IBC and institutional review board, or IRB, of each institution at which we conduct clinical trials of our product candidates, or a central IRB if appropriate, would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any of our product candidates. Similarly, the EMA governs the development of gene therapies in the European Union and may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines. These regulatory review agencies and committees and the new requirements or guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory agencies and committees and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our or our collaborators' ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

If Any Of The Product Candidates We May Develop Or The Delivery Modes We Rely On Cause Undesirable Side Effects, It Could Delay Or Prevent Their Regulatory Approval, Limit The Commercial Potential Or Result In Significant Negative Consequences Following Any Potential Marketing Approval.

Table of Contents

Product candidates we may develop may be associated with undesirable side effects, unexpected characteristics or other serious adverse events, including off-target cuts of DNA, or the introduction of cuts in DNA at locations other than the target sequence. These off-target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA, or, in those instances where we also provide a segment of DNA to serve as a repair template, it is possible that following off-target cut events, DNA from such repair template could be integrated into the genome at an unintended site, potentially disrupting another important gene or genomic element. There also is the potential risk of delayed adverse events following exposure to gene editing therapy due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. Possible adverse side effects that could occur with treatment with gene editing products include an immunologic reaction after administration which could substantially limit the effectiveness of the treatment. Additionally, immunotherapy, and its method of action of harnessing the body's immune system, is powerful and could lead to serious side effects that we only discover in clinical trials. Unforeseen side effects could arise either during clinical development or, if such side effects are more rare, after our product candidates have been approved by regulatory authorities and the approved product has been marketed, resulting in the exposure of additional patients. If our CRISPR/Cas9 gene editing technology demonstrates a similar effect, we may decide or be required to halt or delay preclinical development or clinical development of our product candidates. In addition to serious adverse events or side effects caused by any product candidate we may develop, the administration process or related procedures also can cause undesirable side effects. If any such events occur, our clinical trials could be suspended or terminated.

If in the future we are unable to demonstrate that such adverse events were caused by factors other than our product candidate, the FDA, EMA or other comparable health regulatory authorities could order us to cease further clinical studies of, or deny approval of, any product candidates we are able to develop for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate we may develop, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to identify and develop product candidates, and may harm our business, financial condition, result of operations and prospects significantly.

Additionally, if we successfully develop a product candidate and it receives marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits of treatment with such product candidate outweighs the risks for each potential patient, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive, and more costly than what is typical for the industry. Furthermore, if we or others later identify undesirable side effects caused by any product candidate that we to develop, several potentially significant negative consequences could result, including:

- regulatory authorities may revoke licenses or suspend, vary or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our CRISPR/Cas9 technology and any product candidates we may identify and develop and could have a material adverse effect on our business, financial condition, results of operations and prospects.

If We Experience Delays Or Difficulties In The Enrollment Of Patients In Clinical Trials, Our Receipt Of Necessary Regulatory Approvals Could Be Delayed Or Prevented.

We or our collaborators may not be able to initiate or continue clinical trials for any product candidates we identify or develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or analogous regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial. Enrollment may be particularly challenging for any rare genetically defined diseases we may target in the future. In addition, if patients are unwilling to participate in our gene editing trials because of negative publicity from adverse

events related to the biotechnology, gene therapy or gene editing fields, competitive clinical trials for similar patient populations, clinical trials in competing products, or for other reasons, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of any product candidates we may develop may be delayed. Moreover, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as any product candidates we may develop, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Table of Contents

Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- size of the patient population and process for identifying subjects;
- design of the trial protocol;
- availability and efficacy of approved medications for the disease under investigation;
- availability of genetic testing for potential patients;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- eligibility and exclusion criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial;
- perceived risks and benefits of gene editing and cellular therapies as therapeutic approaches;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Enrollment delays in our clinical trials may result in increased development costs for any product candidates we may develop, which would cause the value of our Company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit, or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, financial condition, results of operations, and prospects.

Positive Results From Early Preclinical Studies Of Our Product Candidates Are Not Necessarily Predictive Of The Results Of Later Preclinical Studies And Any Future Clinical Trials Of Our Product Candidates. If We Cannot Replicate The Positive Results From Our Earlier Preclinical Studies Of Our Product Candidates In Our Later Preclinical Studies And Future Clinical Trials, We May Be Unable To Successfully Develop, Obtain Regulatory Approval For And Commercialize Our Product Candidates.

Any positive results from our preclinical studies of our product candidates may not necessarily be predictive of the results from required later preclinical studies and clinical trials. Similarly, even if we are able to complete our planned preclinical studies or any future clinical trials of our product candidates according to our current development timeline, the positive results from such preclinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical and other nonclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical, non-clinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval.

Even If We Complete The Necessary Preclinical Studies And Clinical Trials, The Marketing Approval Process Is Expensive, Time-Consuming, And Uncertain And May Prevent Us From Obtaining Approvals For The Commercialization Of Any Product Candidates We May Develop. If We Are Not Able To Obtain, Or If There Are Delays In Obtaining, Required Regulatory Approvals, We Will Not Be Able To Commercialize, Or Will Be Delayed In Commercializing, Product Candidates We May Develop, And Our Ability To Generate Revenue Will Be Materially Impaired.

Table of Contents

Any product candidates we may develop and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States, by EMA in the European Union and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval or clearance to market any product candidates from regulatory authorities in any jurisdiction and it is possible that none of our product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval or clearance. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations, or CROs, or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate's safety, purity, efficacy and potency. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any product candidates we develop may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and in other jurisdictions, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. If we experience delays in obtaining approval or if we fail to obtain approval of any product candidates we may develop, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired.

We May Never Obtain FDA Approval For Any Of Our Product Candidates In The United States, And Even If We Do, We May Never Obtain Approval For Or Commercialize Any Of Our Product Candidates In Any Other Jurisdiction, Which Would Limit Our Ability To Realize Their Full Market Potential.

In order to eventually market any of our product candidates in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a jurisdiction-by-jurisdiction basis regarding safety and efficacy. Approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking regulatory approval in multiple jurisdictions could result in difficulties and costs for us and require additional preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in certain countries. Regulatory approval processes outside the United States involve all of the risks associated with FDA approval. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be unrealized.

Gene Editing Products Are Novel And May Be Complex And Difficult To Manufacture. We Could Experience Manufacturing Problems That Result In Delays In The Development Or Commercialization Of Our Product Candidates Or Otherwise Harm Our Business.

The manufacturing process used to produce CRISPR/Cas9-based product candidates may be complex, as they are novel and have not been validated for clinical and commercial production. Several factors could cause production

interruptions, including equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers.

Table of Contents

Our product candidates will require processing steps that are more complex than those required for most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of biologics generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we will employ multiple steps to control the manufacturing process to assure that the process works and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical grade materials that meet FDA, the EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA and other health regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other health regulatory authorities may require that we not distribute a lot until the relevant agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects. Problems in our manufacturing process could restrict our ability to meet market demand for our products.

We also may encounter problems hiring and retaining directly or through contract manufacturing organizations the experienced scientific, quality-control and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements. Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs.

Adverse Public Perception Of Gene Editing And Cellular Therapy Products May Negatively Impact Demand For, Or Regulatory Approval Of, Our Product Candidates.

Our product candidates involve editing the human genome. The clinical and commercial success of our product candidates will depend in part on public acceptance of the use of gene editing therapies for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene editing is unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Negative public reaction to gene therapy in general could result in greater government regulation and stricter labeling requirements of gene editing products, including any of our product candidates, and could cause a decrease in the demand for any products we may develop. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

In particular, gene editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of gene editing technology to human embryos or the human germline. For example, in April 2015, Chinese scientists reported on their attempts to edit the genome of human embryos to modify the gene for hemoglobin beta. This is the gene in which a mutation occurs in patients with the inherited blood disorder beta-thalassemia. Although this research was purposefully conducted in embryos that were not viable, the work prompted calls for a moratorium or other types of restrictions on gene editing of human eggs, sperm, and embryos. The Alliance for Regenerative Medicine in Washington, D.C. has called for a voluntary moratorium on the use of gene editing technologies, including CRISPR/Cas9, in research that involves altering human embryos or human germline cells. Similarly, the NIH has announced that it would not fund any use of gene editing technologies in human embryos, noting that there are multiple existing legislative and regulatory prohibitions against such work, including the Dickey-Wicker Amendment, which prohibits the use of appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed. Laws in the United Kingdom prohibit genetically modified embryos from being implanted into women, but embryos can be altered in research labs under license from the Human Fertilisation and Embryology Authority. Research on embryos is more tightly controlled in many other European countries.

Although we do not use our technologies to edit human embryos or the human germline, such public debate about the use of gene editing technologies in human embryos and heightened regulatory scrutiny could prevent or delay our development of product candidates. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair our development and commercialization of product candidates or demand for any products we may develop. Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing gene editing technologies, even if not ultimately attributable to

Table of Contents

product candidates we may identify and develop, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of potential product candidates we may identify and develop, stricter labeling requirements for those product candidates that are approved, and a decrease in demand for any such product candidates.

If, In The Future, We Are Unable To Establish Sales And Marketing Capabilities Or Enter Into Agreements With Third Parties To Sell And Market Products Based On Our Technologies, We May Not Be Successful In Commercializing Our Products If And When Any Products Candidates Are Approved And We May Not Be Able To Generate Any Revenue.

We do not currently have a sales or marketing infrastructure and, as a company, have no experience in the sale, marketing or distribution of therapeutic products. To achieve commercial success for any approved product candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if any are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future product that we may develop;
- the lack of complementary treatments to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability to us from these revenue streams is likely to be lower than if we were to market and sell any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we may not be successful in commercializing our product candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

Even If We, Or Any Collaborators We May Have, Obtain Marketing Approvals For Any Product Candidates We Develop, The Terms Of Approvals And Ongoing Regulation Of Our Products Could Require The Substantial Expenditure Of Resources And May Limit How We, Or They, Manufacture And Market Our Products, Which Could Materially Impair Our Ability To Generate Revenue.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising, and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, current Good Manufacturing Practice, or cGMP, requirements relating to quality control, quality assurance and corresponding maintenance of records and documents and requirements regarding recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA also may place other conditions on approvals including the requirement for a REMS to assure the safe use

of the product. If the FDA concludes a REMS is needed, the sponsor of the Biologics License Application, or BLA, must submit a proposed REMS before it can obtain approval. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

Table of Contents

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition, and prospects.

Any Product Candidate For Which We Obtain Marketing Approval Could Be Subject To Restrictions Or Withdrawal From The Market, And We May Be Subject To Substantial Penalties If We Fail To Comply With Regulatory Requirements Or If We Experience Unanticipated Problems With Our Products, When And If Any Of Them Are Approved.

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of biologics to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the United States Department of Justice. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown problems with a product candidate, including adverse events of unanticipated severity or frequency, or with our manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on such products, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on the distribution or use of a product;
- requirements to conduct post-marketing clinical trials;
- receipt of warning or untitled letters;
- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory biologic recalls;
- refusal to approve pending applications or supplements to approved applications that we submit;
- fines, restitution, or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals or revocation of biologics licenses;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our products;
- product seizure or detention; and
- injunctions or the imposition of civil or criminal penalties.

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

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may also inhibit

our ability to commercialize any product candidates we may develop and adversely affect our business, financial condition, results of operations, and prospects.

Table of Contents

The Commercial Success Of Any Of Our Product Candidates Will Depend Upon Its Degree Of Market Acceptance By Physicians, Patients, Third-party Payors And Others In The Medical Community.

Ethical, social and legal concerns about gene therapy could result in additional regulations restricting or prohibiting our products. Even with the requisite approvals from FDA in the United States, the EMA in the European Union and other regulatory authorities internationally, the commercial success of our product candidates will depend, in significant part, on the acceptance of physicians, patients and health care payors of gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, patients, health care payors and others in the medical community. The degree of market acceptance of gene therapy products and, in particular, our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy, durability and safety of such product candidates as demonstrated in any future clinical trials;
- the potential and perceived advantages of product candidates over alternative treatments;
- the cost of treatment relative to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA or the EMA;
- patient awareness of, and willingness to seek, genotyping;
- the willingness of physicians to prescribe new therapies;
- the willingness of the target patient population to try new therapies;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of FDA, the EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party payor coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and future clinical trials, market acceptance of the product will not be fully known until after it is launched. If our product candidates do not achieve an adequate level of acceptance following regulatory approval, if ever, we may not generate significant product revenue and may not become profitable.

We May Expend Our Limited Resources To Pursue A Particular Product Candidate Or Indication And Fail To Capitalize On Product Candidates Or Indications That May Be More Profitable Or For Which There Is A Greater Likelihood Of Success.

We have limited financial and managerial resources. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We Face Significant Competition In An Environment Of Rapid Technological Change And The Possibility That Our Competitors May Achieve Regulatory Approval Before Us Or Develop Therapies That Are More Advanced Or Effective

Than Ours, Which May Harm Our Business And Financial Condition, And Our Ability To Successfully Market Or Commercialize Our Product Candidates.

The biotechnology and pharmaceutical industries, including the gene therapy field, are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions, some or all of which may have greater access to capital or resources than we do.

Table of Contents

We are aware of several companies focused on developing gene editing in various indications using CRISPR/Cas9 gene editing technology, including Intellia Therapeutics, Inc. and Editas Medicine, Inc., or Editas. There can be no certainty that other gene editing technologies will not be considered better or more attractive than our technology for the development of products. For example, Editas has exclusively licensed a CRISPR system involving a different protein, Cpf1, which can also edit human DNA as well as advanced forms of Cas9. Editas and certain of its scientific founders have asserted that Cpf1 may work better than Cas9 in some cases. Cas9 may be determined to be less attractive than Cpf1 or other CRISPR proteins that have yet to be discovered.

There are additional companies developing therapies using additional gene editing technologies, including transcription activator-like effector nucleases (TALENs), meganucleases and zinc finger nucleases (ZFNs). These companies include bluebird bio, Cellectis, Poseida Therapeutics, Precision Biosciences, and Sangamo Biosciences. Additional companies developing gene therapy products include Abeona Therapeutics, Avalanche Biotechnologies, Dimension Therapeutics, REGENXBIO, Spark Therapeutics and uniQure.

In addition to competition from other gene editing therapies or gene therapies, any product we may develop may also face competition from other types of therapies, such as small molecule, antibody or protein therapies. In addition, new scientific discoveries may cause CRISPR/Cas9 technology, or gene editing as a whole, to be considered an inferior form of therapy.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical studies, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, have broader acceptance and higher rates of reimbursement by third party payors or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products and our patents may not be sufficient to prevent our competitors from commercializing competing products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

To become and remain profitable, we must develop and eventually commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. These activities can include completing preclinical studies and clinical trials of our product candidates, obtaining marketing and reimbursement approval for these product candidates, manufacturing, marketing and selling those products that are approved and satisfying any post marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our Company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our Company also could cause shareholders to lose all or part of their investment.

Even If We Are Able To Commercialize Any Product Candidates, Such Products May Become Subject To Unfavorable Pricing Regulations, Third-party Reimbursement Practices, Or Healthcare Reform Initiatives, Which Would Harm Our Business.

Table of Contents

The regulations that govern marketing approvals, pricing, and reimbursement for new biologic products vary widely from country to country. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some non-U.S. markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

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

Risks Related to Our Relationships with Third Parties

If Conflicts Arise Between Us And Our Collaborators Or Strategic Partners, These Parties May Act In A Manner Adverse To Us And Could Limit Our Ability To Implement Our Strategies.

If conflicts arise between our corporate or academic collaborators or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Some of our academic collaborators and strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for our product candidates.

Some of our collaborators or strategic partners could also become our competitors in the future. Our collaborators or strategic partners could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, or fail to devote sufficient resources to the development and commercialization of products. Any of these developments could harm our product development efforts.

Our Collaborators Or Strategic Partners May Decide To Adopt Alternative Technologies Or May Be Unable To Develop Commercially Viable Products With Our Technology, Which Would Negatively Impact Our Revenues And Our Strategy To Develop These Products.

Table of Contents

Our collaborators or strategic partners may adopt alternative technologies, which could decrease the marketability of our CRISPR/Cas9 gene editing technology. Additionally, because our current are and we anticipate that any future collaborators or strategic partners will be working on more than one development project, they could choose to shift their resources to projects other than those they are working on with us. If they do so, this would delay our ability to test our technology and would delay or terminate the development of potential products based on our CRISPR/Cas9 gene editing technology. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing or sale of these products. The failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators would prevent us from receiving future milestone and royalty payments which would negatively impact our revenues.

Our Collaborators And Strategic Partners May Control Aspects Of Our Clinical Trials and Commercialization Efforts, Which Could Result In Delays And Other Obstacles In The Commercialization Of Our Proposed Products And Materially Harm Our Results Of Operations.

For some programs, we will depend on third party collaborators and strategic partners to design and conduct our clinical trials, and for any approved products, the commercialization of such products. As a result, we may not be able to conduct these programs in the manner or on the time schedule we currently contemplate, which may negatively impact our business operations. In addition, if any of these collaborators or strategic partners withdraw support for our programs or proposed products or otherwise impair their development or commercialization, our business could be negatively affected. In October 2015, we entered into a four-year collaboration agreement with Vertex to research, develop and commercialize new treatments aimed at the underlying genetic causes of human diseases, including beta-thalassemia and sickle cell. In December 2017, we entered into the JDA with Vertex, initially for the development and commercialization of CTX001 for beta-thalassemia and sickle cell disease. In addition, in December 2015, we entered into an agreement with Bayer Healthcare to create a joint venture to discover and commercialize therapeutics for the treatment of blood disorders, blindness and heart disease in addition to select indications related to other sensory organs, metabolic diseases and autoimmune diseases based on our CRISPR/Cas9 gene editing technology.

We and Bayer Healthcare each hold a 50% interest in the joint venture and each have two designees on the management board. As such, we cannot control all aspects of the clinical development and commercialization of any product candidate developed by the joint venture. Similarly, under our collaboration agreement with Vertex, Vertex has sole authority to select genetic targets to pursue and we will not have control over the development of any product candidates for the selected genetic targets. Under the JDA, we and Vertex have an equal number of representatives on the various committees contemplated by the JDA, which will prevent us from having sole control of the development of CTX001 or any future product candidates subject to the JDA. Furthermore, pursuant to the JDA, Vertex will be solely responsible for the commercialization activities of any approved products subject to the JDA outside of the United States. Our lack of control over the clinical development and commercialization activities in our agreements with Bayer Healthcare and Vertex could cause delays or other difficulties in the development and commercialization of product candidates, which may prevent among other things, completion of intended IND filings for the first clinical trial for our hemoglobinopathy program targeting sickle cell disease in a timely fashion, if at all, or the completion or delay in BLA filings, as well as the timely initiation of clinical trials for beta-thalassemia upon approval of the CTA, if at all.

In addition, the termination of our agreements with Vertex would prevent us from receiving any milestone, royalty payments and other benefits under that agreement. The termination of our joint venture with Bayer Healthcare would prevent us from participating in the profits of the joint venture. Either occurrence would have a materially adverse effect on our results of operations.

We May Seek To Establish Additional Collaborations And, If We Are Not Able To Establish Them On Commercially Reasonable Terms, We May Have To Alter Our Development And Commercialization Plans.

Our product candidate development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any additional collaborations will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and

Table of Contents

complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. For example, we have granted exclusive rights to Vertex for certain genetic targets, and during the term of the collaboration agreement, we will be restricted from granting rights to other parties to use our CRISPR/Cas9 technology to pursue therapies that address these genetic targets. Similarly, pursuant to our joint venture agreement with Bayer Healthcare, during the term of the joint venture, and for a specified period after the termination of the joint venture, we will be prohibited from developing products that use our CRISPR/Cas9 technology in specified fields that would compete with the joint venture and Bayer, respectively. The non-competition provisions in each of these agreements could limit our ability to enter into strategic collaborations with future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If we are unable to negotiate and enter into new collaborations, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We Expect To Rely On Third Parties To Conduct Our Clinical Trials And Certain Aspects Of Our Preclinical Studies For Our Product Candidates. If These Third Parties Do Not Successfully Carry Out Their Contractual Duties, Comply With Regulatory Requirements Or Meet Expected Deadlines, We May Not Be Able To Obtain Regulatory Approval For Or Commercialize Our Product Candidates And Our Business Could Be Substantially Harmed.

We expect to rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct future clinical trials and we currently rely on third parties to conduct certain aspects of our preclinical studies for our product candidates. Nevertheless, we are responsible for ensuring that each of our preclinical studies and any future clinical trials we sponsor are conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards and our reliance on CROs will not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulations, commonly referred to as Good Clinical Practices, or GCPs, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions. For any violations of laws and regulations during the conduct of our preclinical studies and clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

We and our CROs will be required to comply with regulations, including GCPs, for conducting, monitoring, recording and reporting the results of preclinical studies and clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial patients are adequately informed, among other things, of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by FDA, the Competent Authorities of the Member States of the European Economic Area and comparable health regulatory authorities for any drugs in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and FDA or comparable health regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will

determine that any of our future clinical trials will comply with GCPs. In addition, our future clinical trials must be conducted with product candidates produced in accordance with the requirements in cGMP regulations. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action.

Table of Contents

Although we intend to design the clinical trials for our product candidates, CROs will conduct all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical studies and clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

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

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs do not perform preclinical studies and future clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates, or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures.

We Expect To Rely On Third Parties To Manufacture Our Clinical Product Supplies, And We Intend To Rely On Third Parties For At Least A Portion Of The Manufacturing Process Of Our Product Candidates, If Approved. Our Business Could Be Harmed If The Third Parties Fail To Provide Us With Sufficient Quantities Of Product Inputs Or Fail To Do So At Acceptable Quality Levels Or Prices.

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and must rely on outside vendors to manufacture supplies and process our product candidates in connection with any clinical trial we undertake of such product candidates. We have not yet caused any product candidates to be manufactured or processed on a commercial scale and may not be able to do so for any of our product candidates. We will make changes as we work to optimize the manufacturing process, and we cannot be sure that even minor changes in the process will result in therapies that are safe and effective.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA, or other health regulatory agencies in other jurisdictions, pursuant to inspections that will be conducted after we submit an application to the FDA or other health regulatory agencies. We will not control the manufacturing process of, and will be completely dependent on, our contract manufacturing partners for compliance with regulatory requirements, known as cGMP requirements, for manufacture of our product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable health regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

Our Relationships With Healthcare Providers, Physicians, And Third-party Payors Will Be Subject To Applicable Anti-kickback, Fraud And Abuse And Other Healthcare Laws And Regulations, Which Could Expose Us To Criminal Sanctions, Civil Penalties, Exclusion From Government Healthcare Programs, Contractual Damages, Reputational Harm And Diminished Profits And Future Earnings.

Although we do not currently have any drugs on the market, once we begin commercializing our product candidates, if ever, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the

U.S. federal government and states as well as other national, regional or local governments in other jurisdictions in which we conduct our business.

Table of Contents

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

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, or recommendation of, any good or service, for which payment may be made under a state or Federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violation of the statute may give rise to criminal and/or civil penalties;
- the federal civil and criminal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid, or other government payors that are false, fictitious or fraudulent or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $5,500 to $11,000 per false claim. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as further amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations which impose certain requirements on covered entities, including healthcare providers, health plans and healthcare clearing houses, as well as their business associates that perform certain services with respect to safeguarding the privacy, security and transmission of individually identifiable health information that constitutes protected health information, including mandatory contractual terms and restrictions on the use and/or disclosure of such information without appropriate authorization;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal physician payment transparency requirements, sometimes referred to as the “Sunshine Act” under the Affordable Care Act, require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program to report to the Department of Health and Human Services information related to physician payments and other transfers of value to physicians and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and
- analogous laws and regulations in U.S. states, and in other countries, regions or localities in which we may do business, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Table of Contents

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including activities that may be conducted by sales and marketing team we establish, are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs. Liabilities they incur pursuant to these laws could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business

Our Future Success Depends On Our Ability To Retain Key Executives And To Attract, Retain And Motivate Qualified Personnel.

We are highly dependent on the research and development, clinical, commercial and business development expertise of Dr. Samarth Kulkarni, our Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. The loss of the services of our executive officers or other key employees or consultants could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. For example, since our IPO our former Chief Executive Officer resigned in his role as Chief Executive Officer and became our President and Chairman of the Board of Directors and our former Chief Financial Officer resigned. While we have promoted Samarth Kulkarni as our new Chief Executive Officer and hired Michael Tomsicek as our new Chief Financial Officer, there is no assurance that we will be able to find qualified replacements in a timely manner, if at all, in the event of the departure of other executive officers or key employees. If we are unable to retain high quality personnel, our ability to pursue our growth strategy will be limited.

We will also need to recruit and retain qualified scientific, clinical and commercial personnel as we advance the development of our product candidates and product pipeline. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific, clinical and commercial personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

In addition, being domiciled and organized in Switzerland may restrict our ability to attract, motivate and retain the required level of qualified personnel. In Switzerland, in 2013 legislation was adopted affecting compensation payable by public companies to members of its board of directors and executive team. Among other things, such legislation (i) imposes an annual binding shareholders' "say on pay" vote with respect to the compensation of executive management, including executive officers and the board of directors; (ii) prohibits severance, advances, transaction premiums and similar payments to executive officers and directors; and (iii) requires companies to specify various compensation-related matters in their articles of association, thus requiring them to be approved by a shareholders' vote.

We Will Need To Develop And Expand Our Company, And We May Encounter Difficulties In Managing This Development And Expansion, Which Could Disrupt Our Operations.

Table of Contents

As of December 31, 2016, we had 93 full-time employees and we expect to increase our number of employees and the scope of our operations in 2017 and beyond as we conduct activities as a public company and seek to advance development and if successful, commercialization, of our product candidates. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these expansion activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

Our Employees, Principal Investigators, Consultants And Commercial Partners May Engage In Misconduct Or Other Improper Activities, Including Non-compliance With Regulatory Standards And Requirements And Insider Trading.

We are exposed to the risk of fraud or other misconduct by our employees, consultants, and commercial partners, and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission, and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and in other jurisdictions, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations, and prospects, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

If We Fail To Comply With Environmental, Health And Safety Laws And Regulations, We Could Become Subject To Fines Or Penalties Or Incur Costs That Could Harm Our Business.

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

Although we anticipate obtaining product liability insurance coverage in advance of the commencement of any clinical trial of our product candidates, it may not be adequate to cover all liabilities that we may incur. Further, we anticipate that we will need to increase our insurance coverage if we successfully commercialize any product candidate. Insurance

coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Table of Contents

Product Liability Lawsuits Against Us Could Cause Us To Incur Substantial Liabilities And Could Limit Commercialization Of Any Product Candidates That We May Develop.

We will face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any product candidates that we may develop. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any product candidates that we may develop.

Although we anticipate obtaining product liability insurance coverage in advance of the commencement of any clinical trial of our product candidates, it may not be adequate to cover all liabilities that we may incur. Further, we anticipate that we will need to increase our insurance coverage if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If We Fail To Establish And Maintain Proper And Effective Internal Control Over Financial Reporting, Our Operating Results And Our Ability To Operate Our Business Could Be Harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. We have begun the process of documenting, reviewing and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act of 2002, or SOX, which will require annual management assessment of the effectiveness of our internal control over financial reporting.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our common share price and make it more difficult for us to effectively market and sell our service to new and existing customers.

Our Internal Computer Systems, Or Those Of Our Collaborators Or Other Contractors Or Consultants, May Fail Or Suffer Security Breaches, Which Could Result In A Material Disruption Of Our Product Development Programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Table of Contents

Our Business Is Subject To Economic, Political, Regulatory And Other Risks Associated With International Operations.

Our business is subject to risks associated with conducting business internationally. We and a number of our suppliers and collaborative and clinical study relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing regulatory requirements for drug approvals in non-U.S. countries;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling outside the United States;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities outside the United States; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including floods and fires.

Our Business Operations Have a Substantial International Footprint and We May Further Expand In The Future, Which Presents Challenges In Managing Our Business Operations.

We are headquartered in Zug, Switzerland and have offices in the U.S. and the United Kingdom. In addition, we may expand our international operations into other countries in the future. While we have acquired significant management and other personnel with substantial experience, conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects, including, among other things:

- the increased complexity and costs inherent in managing international operations;
- diverse regulatory, financial and legal requirements, and any future changes to such requirements, in one or more countries where we are located or do business;
- country-specific tax, labor and employment laws and regulations;
- challenges inherent in efficiently managing employees in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and other regulations;
- liabilities for activities of, or related to, our international operations or product candidates;
- changes in currency rates; and
- regulations relating to data security and the unauthorized use of, or access to, commercial and personal information.

As we continue to expand our operations, our corporate structure and tax structure has become substantially more complex. In connection with our current and future potential partnerships, we are actively engaged in developing and applying

technologies and intellectual property with a view toward commercialization of products globally, often with commercialization partners. In connection with those activities, we already have and will likely continue to engage in complex cross-border and global transactions involving our technology, intellectual property and other assets, between CRISPR and other entities such as partners and licensees, and between companies within the CRISPR group. Such cross-border and global arrangements are both difficult to manage and can potentially give rise to complexities in areas such

Table of Contents

as tax treatment, particularly since we are subject to multiple tax regimes and different tax authorities can also take different views from each other, even as regards the same cross-border transaction or arrangement. There can be no assurance that we will effectively manage this increased complexity without experiencing operating inefficiencies, control deficiencies or tax liabilities. Significant management time and effort is required to effectively manage the increased complexity of our company, and our failure to successfully do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Risks Related to Intellectual Property

If We Are Unable To Adequately Protect Our Proprietary Technology Or Obtain And Maintain Patent Protection For The Products We Develop And For Our Technology And Product Candidates, Or If The Scope Of The Patent Protection Obtained Is Not Sufficiently Broad, Our Competitors Could Develop And Commercialize Products And Technology Similar Or Identical To Ours, And Our Ability To Successfully Commercialize Any Product Candidates We May Develop, And Our Technology May Be Adversely Affected.

Our success depends in large part on our ability to obtain and maintain proprietary or intellectual property protection in the United States and other countries with respect to our CRISPR/Cas9 platform technology and any proprietary product candidates and technology we develop. Currently, no patents covering our CRISPR/Cas9 platform or product candidates have been issued to us in the United States and one of the patent applications we have licensed that may cover our platform was the subject of an interference proceeding at the United States Patent and Trademark Office, or USPTO; the termination of the interference proceeding has been appealed to the U.S. Court of Appeals for the Federal Circuit, or Federal Circuit, as discussed below. One patent covering our CRISPR/Cas9 platform was issued in Europe, but is the subject of opposition proceedings. We seek to protect our proprietary position by in-licensing intellectual property to cover our platform technology and filing patent applications in the United States and in other jurisdictions related to our technologies and product candidates that are important to our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position. If we or our licensors are unable to obtain or maintain patent protection with respect to our CRISPR/Cas9 platform technology and any proprietary products and technology we develop, our business, financial condition, results of operations and prospects could be materially harmed.

The scope of patent protection that will be available to us in the United States and in other countries is uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors, or if any such patents will be found invalid, unenforceable or not infringed if challenged by our competitors.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with any degree of certainty whether the inventors of our licensed patents and applications were the first to make the inventions claimed in our owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates.

Table of Contents

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we hold or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether any of our platform advances and product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. For example, we are aware that third parties have suggested the use of the CRISPR technology in conjunction with a protein other than Cas9. Our owned and in-licensed patents may not cover such technology. If our competitors commercialize the CRISPR technology in conjunction with a protein other than Cas9, our business, financial condition, results of operations, and prospects could be materially adversely affected.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability and our patents may be challenged in the courts or patent offices in the United States and in other jurisdictions. We may be subject to a third party preissuance submission of prior art to the USPTO, or a patent office in another jurisdiction, or become involved in opposition, derivation, revocation, reexamination, post-grant review and inter partes review, or interference proceedings, or litigation challenging our patent rights or the patent rights of others. Indeed, certain of our fundamental intellectual property has been subject to third party observations outside the United States and interference proceedings within the United States. Competitors may claim that they invented the inventions claimed in such issued patents or patent applications prior to our inventors, or may have filed patent applications before our inventors did. A competitor may also claim that our products and services infringe its patents and that we therefore cannot practice our technology as claimed under our patent applications, if issued. An adverse determination in any such claim may result in our inability to manufacture or commercialize products without infringing third-party patent rights. Competitors may also contest our patents, if issued, by showing that the invention was not patent-eligible, was not novel, was obvious or that the patent claims failed any other requirement for patentability. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights or allow third parties to commercialize our technology or products and compete directly with us, without payment to us. Moreover, we, or one of our licensors, may have to participate in additional interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a non-U.S. patent office, that challenge priority of invention or other features of patentability. Such challenges may result in loss of patent rights, loss of exclusivity or freedom to operate, or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

We Are Required To Pay Royalties Under Our License Agreements With Third-Party Licensors, And We Must Use Commercially Reasonable Diligence Efforts And Meet Milestones To Maintain Our License Rights.

Under our in-license agreements, including our in-license agreements with Dr. Emmanuelle Charpentier, we will be required to pay royalties based on our revenues from sales of our products utilizing the licensed technologies and these royalty payments could adversely affect the overall profitability for us of any products that we may seek to commercialize. Under each of our in-license agreements with, Dr. Charpentier, we have an obligation to use commercially reasonable efforts to develop and obtain regulatory approval to market a licensed therapeutic product. Our in-license agreements with Dr. Charpentier also include an obligation to file a U.S. Investigational New Drug application (or its equivalent in a major market country) by April 2021 and an obligation to file a U.S. Investigational New Drug application (or its equivalent in a major market country) by April 2024. We may not be successful in meeting these obligations in the future on a timely basis or at all. Our failure to meet these obligations may give Dr. Charpentier the right to terminate our license rights. We will need to outsource and rely on third parties for many aspects of the clinical development of the products covered under our license agreements. Delay or failure by these third parties could adversely affect our ability to meet our diligence obligations and the continuation of our license agreements with third-party licensors.

Some Of Our In-licensed Patent Applications Are Subject To Priority Disputes And Inventorship Disputes And Our Owned And In-Licensed Patents And Other Intellectual Property May Be Subject To Further Priority Disputes Or To Inventorship Disputes And Similar Proceedings. If We Or Our Licensors Are Unsuccessful In Any Of These Proceedings, We May Be Required To Obtain Licenses From Third Parties, Which May Not Be Available On Commercially Reasonable Terms Or

At All, Or To Cease The Development, Manufacture, And Commercialization Of One Or More Of The Product Candidates We May Develop, Which Could Have A Material Adverse Impact On Our Business.

Table of Contents

In January 2016, at our request, the USPTO declared an interference between one of the pending U.S. patent applications we licensed from Dr. Charpentier and twelve issued U.S. patents, and subsequently added one U.S. patent application, owned jointly by the Broad Institute and Massachusetts Institute of Technology and, in some instances, the President and Fellows of Harvard College, collectively referred to as the Broad. An interference is a proceeding conducted at the USPTO by the Patent Trial and Appeal Board, or PTAB, to determine which party was the first to invent subject matter claimed by both of these parties. There were two parties to this interference. Because our application was filed first, the USPTO designated Dr. Charpentier, the Regents of the University of California, or California, and the University of Vienna, or Vienna, collectively as "Senior Party" and designated Broad as "Junior Party." Following motions by the parties and other procedural matters, the PTAB concluded in February 2017 that the declared interference should be dismissed because the claim sets of the two parties were not directed to the same patentable invention in accordance with the PTAB's two-way test for patent interferences. In particular, the Junior Party's claims in the interference were all limited to uses in eukaryotic cells, while the Senior Party's claims in the interference were not limited to uses in eukaryotic cells but included uses in all settings. In April 2017, the Senior Party appealed the PTAB decision to the Federal Circuit, seeking review and reversal of the PTAB's February 2017 decision, which terminated the interference without determining which inventors actually invented the use of the CRISPR/Cas9 genome editing technology in eukaryotic cells. In parallel, either party can pursue existing or new patent applications in the U.S. and elsewhere. For example, one of the Broad's pending patent applications (U.S. Serial No. 14/523,799) is scheduled to issue as U.S. Patent No. 9,840,713 on December 12, 2017. Going forward, either party as well as other parties could seek a new interference related to the uses of the technology in eukaryotic cells or other aspects of the technology, and any existing or new patents could be the subject of other challenges to their validity of enforceability. In the context of a second interference or in other proceedings, a determination could be reached regarding that the Senior Party was not the first to invent, or it could be concluded that the contested subject matter is not patentable to the Senior Party and is patentable to the Junior Party, which in this case could preclude our U.S. patent applications from issuing as patents, in which case the proceedings would result in our losing the right to protect core innovations and our freedom to practice our core gene editing technology. If there is a second interference, either party can again appeal an adverse decision to the U.S. Court of Appeals for the Federal Circuit. In any case, it may be years before there is a final determination on priority. Pursuant to the terms of the license agreement with Dr. Charpentier, we are responsible for covering or reimbursing Dr. Charpentier's patent prosecution defense and related costs associated with our in-licensed technology.

Furthermore, we may be involved in other interference proceedings or other disputes in the future. For example, Toolgen Inc., or Toolgen, filed Suggestions of Interference in the USPTO on April 13, 2015, and December 3, 2015, suggesting that they believe some of the claims in pending U.S. applications owned by Toolgen (U.S. Serial No. 14/685,568 and U.S. Serial No. 14/685,510, respectively) interfere with certain claims in five of the Broad patents currently involved in the interference with Dr. Charpentier, California and Vienna. The USPTO may, in the future, declare an interference between our patent application and one or more Toolgen patent applications. We are also aware of additional third parties that have pending patent applications relating to CRISPR technologies, which similarly may or may not lead to further interference proceedings. For example, Rockefeller University has filed an application (U.S. Serial No. 15/217,489) claiming priority to an application filed by the Broad, but which names Rockefeller's employee Luciano Marraffini as co-inventor of CRISPR/Cas9 technology; Vilnius University has filed applications in the United States and in other jurisdictions (published internationally as WO2013/141680 and WO2013/142578 and granted as a patent in the United States as U.S. Patent No. 9,637,739), Harvard University has filed applications in the United States and in other jurisdictions (published internationally as WO2014/099744 and granted as a patent in the United States as U.S. Patent No. 9,023,649), and Sigma-Aldrich has filed applications in the United States and in other jurisdictions (published internationally as WO2014/089290), each claiming aspects of CRISPR/Cas9 technology based on applications claiming priority to provisional filings in 2012. Numerous other filings are based on provisional applications filed after 2012.

Broad, Toolgen, Vilnius, Harvard, Sigma-Aldrich and other parties routinely file international counterparts of their U.S. applications, some of which have been granted or could in future be granted in Europe and/or other non-U.S. jurisdictions. We and third parties have initiated opposition proceedings against some of these grants, and we may in the future oppose other grants to these or other applicants. For example, we and eight other entities have opposed European Patent 2771468 that was granted to Broad, MIT and Harvard. A hearing is scheduled for January 16, 2018 to determine the outcome of the opposition. Similarly, our intellectual property may in the future become involved in opposition proceedings in Europe or other jurisdictions. For example, the issued European patent we in-licensed from Dr. Charpentier has already been opposed by two third parties, and additional third parties may file oppositions to that patent in the future. The opposition to the European patent could lead to the revocation of the patents in whole or in part, or could lead to the claims being narrowed in a way that could impair or preclude our ability to enforce the patent against competitors in Europe.

If we or our licensors are unsuccessful in any interference proceedings or other priority or validity disputes (including any patent oppositions) to which we or they are subject or become subject to, we may lose valuable intellectual property rights through the loss or narrowing of one or more of our patent applications. If we or our licensors are unsuccessful in any interference proceeding or other dispute, we may be required to seek to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other disputes. These third parties would be under no obligation to grant to us any such license and such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we and our partners may need to

Table of Contents

cease the practice of our core gene editing, and the development, manufacture, and commercialization of one or more of the product candidates we may develop. The loss of exclusivity or the narrowing of our patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products. Any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations, or prospects. If we are unsuccessful in our dispute with Broad, we and our partners may be blocked from commercializing any products based on our core gene editing technology. Even if we are successful in an interference proceeding or other similar disputes, it could result in substantial costs and be a distraction to management and other employees.

The Intellectual Property That Protects Our Core Gene Editing Technology Is Jointly Owned, And Our License Is From Only One Of The Joint Owners, Materially Limiting Our Rights In The United States And In Other Jurisdictions.

The family of patent applications we have in-licensed from Dr. Charpentier is the foundational patent protection for our core gene editing technology. However, that family includes other named inventors who assigned their rights either to California or to Vienna. As such, the intellectual property is currently co-owned by Dr. Charpentier, California, and Vienna. On December 15, 2016, we entered into a Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement, or IMA, with California, Vienna and their licensees including Caribou Biosciences, Inc. and Caribou's licensee Intellia Therapeutics, Inc. Under the IMA, the co-owners provided reciprocal worldwide cross-consents to each of the other co-owners' licensees and sublicensees, and agreed to a number of other commitments and obligations with respect to supporting and managing the underlying CRISPR/Cas9 gene editing intellectual property, including a cost-sharing agreement. As explained more fully below, that leaves us in a position of holding only non-exclusive or co-exclusive rights to the patent rights that protect our core gene editing technology, and we must continue to satisfy our contractual obligations under the IMA in order to maintain the effectiveness of the consents by California and Vienna to our license from Dr. Charpentier.

In the United States, each co-owner has the freedom to license and exploit the technology. As a result, we do not have exclusive access to any intellectual property rights that Dr. Charpentier co-owns with another entity, such as California and Vienna. Our license with Dr. Charpentier is therefore non-exclusive with respect to such co-owned rights. Furthermore, in the United States each co-owner is required to be joined as a party to any claim or action we may wish to bring to enforce those patent rights. Moreover, in the United States, non-exclusive licenses have no standing to bring a patent infringement action before a court. Therefore, for the patents owned with California and Vienna we have no ability to pursue third party infringement claims without cooperation of California and Vienna and potentially their licensees. Although we have entered into a Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement with Vienna and California and their licensees, which provides for, among other things, notice of and coordination in the event of third-party infringement of the CRISPR/Cas9 intellectual property, there can be no assurance that Vienna and California will cooperate with us in any future infringement. If we are unable to enforce our core patent rights licensed from Dr. Charpentier, we may be unable to prevent third parties from competing with us and may be unable to persuade companies to sublicense our technology, either of which could have a material adverse effect on our business.

If We Experience Disputes With The Third Parties That We In-license Intellectual Property Rights From, We Could Lose License Rights That Are Important To Our Business.

We license our foundational intellectual property from a third party, and we expect to continue to in-license additional third-party intellectual property rights as we expand our CRISPR/Cas9 gene-editing technology. Disputes may arise with the third parties from whom we license our intellectual property rights from for a variety of reasons, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships and obligations associated with sublicensing;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties, or maintain consents under the IMA, are complex, and certain provisions in such agreements may be susceptible to multiple interpretations, or may conflict in such a way that puts us in breach of one or more agreements, which would make us

Table of Contents

susceptible to lengthy and expensive disputes with one or more of our licensing partners or the parties to the IMA. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

We May Not Be Successful In Obtaining Necessary Rights To Any Product Candidates We May Develop Through Acquisitions And In-licenses.

We currently have rights to intellectual property, through in-licenses from third parties, to identify and develop product candidates. Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the field of gene-editing technology and filing patent applications potentially relevant to our business. For example, we are aware of several third party patent applications that, if issued, may be construed to cover our CRISPR/Cas9 technology and product candidates. In order to avoid infringing these third party patents, we may find it necessary or prudent to obtain licenses from such third party intellectual property holders. We may also require licenses from third parties for certain modified or improved components of CRISPR/Cas9 technology, such as modified nucleic acids, as well as non-CRISPR/Cas9 technologies such as delivery methods that we are evaluating for use with product candidates we may develop. In addition, with respect to any patents we co-own with third parties, we may require licenses to such co-owners' interest to such patents. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for product candidates we may develop and CRISPR/Cas9 technology. The licensing or acquisition of third party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, or discontinue the practice of our core CRISPR/Cas9 gene-editing technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Issued Patents Covering Our Technology And Product Candidates Could Be Found Invalid Or Unenforceable If Challenged In Court.

If we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering a product candidate we may develop or our technology, including CRISPR/Cas9, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement.

Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties have raised challenges to the validity of certain of our in-licensed patent applications, such as our in-licensed CRISPR/Cas9 patent applications in the context of third party observations and oppositions filed in Europe and Australia, and may in the future raise similar claims before administrative bodies in the United States or in other jurisdictions, even outside the context of litigation. Mechanisms for challenging the validity of patents in patent offices include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in non-U.S. jurisdictions (e.g., opposition proceedings). Such proceedings could result in the loss of our patent applications or patents, or their narrowing in such a way that they no longer cover our technology or platform, or any product candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our

technology or platform, or any product candidates that we may develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and prospects.

Table of Contents

The Intellectual Property Landscape Around Gene-Editing Technology, Including CRISPR/Cas9, Is Highly Dynamic, And Third Parties May Initiate And Prevail In Legal Proceedings Alleging That The Patents That We In-License Or Own Are Invalid Or That We Are Infringing, Misappropriating, Or Otherwise Violating Their Intellectual Property Rights, The Outcome Of Which Would Be Uncertain And Could Have A Material Adverse Effect On The Success Of Our Business.

The field of gene editing, especially in the area of CRISPR/Cas9 technology, is still in its infancy, and no such products have reached the market. Due to the intense research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain for the coming years. There may be significant intellectual property related litigation and proceedings, in addition to the ongoing interference proceedings, relating to our owned and in-licensed, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market, and sell any product candidates that we may develop and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. We are subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and any product candidates we may develop, including re-examination interference proceedings, post-grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in other jurisdictions such as oppositions before the European Patent Office. Third parties, including parties involved in ongoing interference proceedings, may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. We are aware of certain third party patents and patent applications including, for example, the Broad, Vilnius, Harvard and Sigma-Aldrich patents described above, that may be asserted to encompass our CRISPR/Cas9 technology. If we are unable to prove that these patents are invalid and we are not able to obtain or maintain a license on commercially reasonable terms, such third parties could potentially assert infringement claims against us, which could have a material adverse effect on the conduct of our business. If we are found to infringe such third party patents, we and our partners may be required to pay damages, cease commercialization of the infringing technology, including our core CRISPR/Cas9 gene-editing technology, or obtain a license from such third parties, which may not be available on commercially reasonable terms or at all. Additionally we have not performed any freedom-to-operate analysis on specific product candidates at this stage to identify potential infringement risks. A proper analysis of that type will not be feasible until specific product candidates are designed.

Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, ownership, or priority. A court of competent jurisdiction could hold that these third party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize any product candidates we may develop and any other product candidates or technologies covered by the asserted third party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe a third party's intellectual property rights, and we are unsuccessful in demonstrating that such patents are invalid or unenforceable, we could be required to obtain a license from such third party to continue developing, manufacturing, and marketing any product candidates we may develop and our technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We also could be forced, including by court order, to cease developing, manufacturing, and commercializing the infringing technology or product candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects.

Intellectual Property Litigation Could Cause Us To Spend Substantial Resources And Distract Our Personnel From Their Normal Responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities and generally harm our business.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation in certain countries, including the United States, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

Table of Contents

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing or misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining And Maintaining Our Patent Protection Depends On Compliance With Various Procedural, Document Submission, Fee Payment, And Other Requirements Imposed By Government Patent Agencies And Our Patent Protection Could Be Reduced Or Eliminated For Non-compliance With These Requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. In certain circumstances, we rely on our licensing partners to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and other patent agencies over the lifetime of the patent. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, we may not be able to stop a competitor from marketing drugs that are the same as or similar to our product candidates, which would have a material adverse effect on our business.

Some Intellectual Property Which We Have In-licensed May Have Been Discovered Through Government Funded Programs And Thus May Be Subject To Federal Regulations Such As "march-in" Rights, Certain Reporting Requirements And A Preference For U.S.-based Manufacturers. Compliance With Such Regulations May Limit Our Exclusive Rights, And Limit Our Ability To Contract With Non-U.S. Manufacturers.

The intellectual property rights to which we have in-licensed under Dr. Charpentier's joint interest are co-owned by California, which has indicated that the invention was made under Grant No. GM081879 awarded by the National Institute of Health. These rights are therefore subject to certain federal regulations. The U.S. government has certain rights pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act, to patents covering government rights in certain inventions developed under a government-funded program. These rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as "march-in rights." The U.S. government also has the right to take title to these inventions if we, or the applicable contractor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable contractor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future patents covering inventions is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

We May Not Be Able To Protect Our Intellectual Property And Proprietary Rights Throughout The World.

Table of Contents

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in intellectual property laws various jurisdictions worldwide. Additionally, the patent laws of some countries do not afford intellectual property protection to the same extent as the laws of the United States. For example, unlike patent law in the United States, the patent law in Europe and many other jurisdictions precludes the patentability of methods of treatment of the human body and imposes substantial restrictions on the scope of claims it will grant if broader than specifically disclosed embodiments.

Many companies have encountered significant problems in protecting and defending intellectual property rights in various jurisdictions globally. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in various jurisdictions globally could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Changes To The Patent Law In The United States And Other Jurisdictions Could Diminish The Value Of Patents In General, Thereby Impairing Our Ability To Protect Our Product Candidates.

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

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. For example, in *Association for Molecular Pathology v. Myriad Genetics, Inc*., the Supreme Court ruled that a "naturally occurring DNA

segment is a product of nature and not patent eligible merely because it has been isolated," and invalidated Myriad Genetics's claims on the isolated BRCA1 and BRCA2 genes. Certain claims of our patents relate to CRISPR/Cas9 gene-editing technology as well as guide components that are directed to naturally occurring DNA sequences. To the extent that such

Table of Contents

claims are deemed to be directed to natural products, or to lack an inventive concept above and beyond an isolated natural product, a court may decide the claims are invalid under *Myriad*. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Europe's planned Unified Patent Court may particularly present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. While that new court is being implemented to provide more certainty and efficiency to patent enforcement throughout Europe, it will also provide our competitors with a new forum to use to centrally revoke our European patents. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by that court. We will have the right to opt our patents out of that system over the first seven years of the court, but doing so may preclude us from realizing the benefits of the new unified court.

If We Are Unable To Protect The Confidentiality Of Our Trade Secrets, Our Business And Competitive Position Would Be Harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. Trade secrets and know-how can be difficult to protect. In particular, we anticipate that with respect to our technology platform, these trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

If We Do Not Obtain Patent Term Extension And Data Exclusivity For Any Product Candidates We May Develop, Our Business May Be Materially Harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or if the term of any such extension is less than we request, we will be unable to rely on our patent position to forestall the marketing of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

Intellectual Property Rights Do Not Necessarily Address All Potential Threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

Table of Contents

- others may be able to make gene therapy products that are similar to any product candidates we may develop or utilize similar gene therapy technology but that are not covered by the claims of the patents that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending licensed patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We May Be Subject To Claims That Our Employees, Consultants, Or Advisors Have Wrongfully Used Or Disclosed Alleged Trade Secrets Of Their Current Or Former Employers Or Claims Asserting Ownership Of What We Regard As Our Own Intellectual Property.

Many of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Our Common Shares and this Offering

The Price Of Our Common Shares Historically Has Been And May In The Future Be Volatile And Fluctuate Substantially, Which May Affect The Price At Which You Could Sell The Common Shares.

Our share price has been and in the future may be subject to substantial volatility. In addition, the stock market in general, and Nasdaq listed and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. For example, our shares traded within a range of a high price of $27.39 and a low price of $11.63 per share for the period beginning on October 19, 2016, our first day of trading on the Nasdaq Global Market, through January 2, 2018. As a result of this volatility, our shareholders could incur substantial losses. In addition, the market price for our common shares may be influenced by many factors, including:

Table of Contents

- the success of existing or new competitive products or technologies;
- the timing and results of any product candidates that we may develop;
- commencement or termination of collaborations for our product development and research programs;
- failure or discontinuation of any of our product development and research programs;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- developments or changing views regarding the use of genomic products, including those that involve gene editing;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common shares by us, our insiders, or other shareholders;
- expiration of market stand-off or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our common shares;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

These and other market and industry factors may cause the market price and demand for our common shares to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their common shares and may otherwise negatively affect the liquidity of our common shares. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our shareholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

We Have Broad Discretion In How We Use The Proceeds Of This Offering And May Not Use These Proceeds Effectively, Which Could Affect Our Results Of Operations And Cause Our Common Share Price To Decline.

We will have considerable discretion in the application of the net proceeds of this offering. We anticipate that we will use the net proceeds from this offering to fund clinical development of CTX001, and CTX101 progress additional pipeline candidates, and to further optimize our CRISPR/Cas9 gene editing platform and delivery technologies as well as for manufacturing, working capital and general corporate purposes, which may include funding for the hiring of additional personnel, capital expenditures. As a result, investors will be relying upon management’s judgment with only limited information about our specific intentions for the use of the balance of the net proceeds of this offering. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our shareholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

Table of Contents

We Are An "Emerging Growth Company," And The Reduced Disclosure Requirements Applicable To Emerging Growth Companies May Make Our Common Shares Less Attractive To Investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of our initial public offering in October 2016; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, which means the market value of our common shares that is held by non-affiliates exceeds $700 million as of the prior June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of SOX;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- being permitted to present only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this prospectus;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens in this prospectus and the documents incorporated by reference into this prospectus. We cannot predict whether investors will find our common shares less attractive if we rely on these exemptions. If some investors find our common shares less attractive as a result, there may be a less active trading market for our common shares and our common share price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Our Executive Officers, Directors, Principal Shareholders And Their Affiliates Maintain The Ability To Exercise Significant Influence Over Our Company And All Matters Submitted To Shareholders For Approval.

The holdings of our executive officers, directors and shareholders who own more than 5% of our outstanding common shares, together with their affiliates and related persons, represent beneficial ownership, in the aggregate, of approximately 66.8% of our common shares, based on the number of common shares outstanding as September 30, 2017. Upon the closing of this offering, the holdings of our executive officers, directors and shareholders who owned more than 5% of our outstanding common shares before this offering, together with their affiliates and related persons, will represent beneficial ownership, in the aggregate, of approximately 59.6% of our common shares (approximately 58.6% if the underwriters exercise in full their option to purchase additional shares), based on the number of common shares outstanding as September 30, 2017. As a result, these shareholders, if they choose to act together, will be able to influence our management and affairs and the outcome of matters submitted to our shareholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other shareholders may desire.

Table of Contents

In addition, this concentration of ownership might adversely affect the market price of our common shares by:

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

If You Purchase Our Common Shares In This Offering, You Will Incur Immediate And Substantial Dilution In The Book Value Of Your Shares.

Investors purchasing common shares in this offering will pay a price per share that substantially exceeds the as adjusted book value per share of our tangible assets as of September 30, 2017 after subtracting our liabilities. As a result, investors purchasing common shares in this offering will incur immediate dilution of $16.54 per share, based on the difference between the public offering price of $22.75 per share and the as adjusted net tangible book value per share of our outstanding common shares as of September 30, 2017.

This dilution is due to the substantially lower price paid by some of our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise of stock options granted to our employees. In addition, as of September 30, 2017, options to purchase 5,778,629 common shares at a weighted average exercise price of $12.36 per share were outstanding. The exercise of any of these options would result in additional dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. Further, because we will need to raise additional capital to fund our future activities, we may in the future sell substantial amounts of common shares or securities convertible into or exchangeable for common shares.

These future issuances of common shares or common share-related securities, together with the exercise of outstanding options and any additional shares issued in connection with acquisitions, if any, may result in further dilution. For a further description of the dilution that you will experience immediately after this offering, see “Dilution.”

Sales Of A Substantial Number Of Our Common Shares In The Public Market Could Cause Our Share Price To Fall.

Sales of a substantial number of our common shares in the public market or the perception that these sales might occur could depress the market price of our common shares, could make it more difficult for you to sell your common shares at a time and price that you deem appropriate and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common shares.

As of September 30, 2017, 40,890,954 common shares were outstanding, including 64,227 issued but unvested restricted shares that are not considered outstanding for accounting purposes until vested and options to purchase 5,778,629 common shares, of which 1,411,943 were exercisable as of that date. The sale or the availability for sale of a large number of our common shares in the public market could cause the price of our common shares to decline. We, along with certain of our executive officers, directors and other shareholders, have agreed that for a period of 90 days after the date of this prospectus supplement, subject to specified exceptions described in the section titled “Underwriting,” we or they will not offer, sell, contract to sell, pledge, or otherwise dispose of, directly or indirectly, any common shares or securities convertible into or exchangeable or exercisable for any common shares. We refer to such period as the lock-up period. This lock-up period affects approximately 15.7 million common shares as of September 30, 2017, representing approximately 38.5% of our outstanding common shares as of that date and prior to giving effect to this offering. When this lock-up period expires, we and our shareholders subject to a lock-up agreement will be able to sell our shares in the public market. In addition, Goldman Sachs & Co. LLC, Piper Jaffray & Co. and Barclays Capital Inc. may release all or some portion of the shares subject to lock-up agreements at any time and for any reason. Sales of a substantial number of such shares upon expiration of the lock-up, the perception that such sales may occur or early release of these agreements could cause our market price to fall or make it more difficult for you to sell your common shares at a time and price that you deem appropriate.

Table of Contents

Certain holders of common shares are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these shareholders could have a material adverse effect on the trading price of our common shares.

The Market Price Of Our Common Shares May Be Adversely Affected By Market Conditions Affecting The Stock Markets In General, Including Price And Trading Fluctuations On The Nasdaq Global Market.

Market conditions may result in volatility in the level of, and fluctuations in, market prices of stocks generally and, in turn, our common shares and sales of substantial amounts of our common shares in the market, in each case being unrelated or disproportionate to changes in our operating performance. The overall weakness in the economy has recently contributed to the extreme volatility of the markets which may have an effect on the market price of our common shares.

We Do Not Expect To Pay Dividends In The Foreseeable Future.

We have not paid any dividends since our incorporation. Even if future operations lead to significant levels of distributable profits, we currently intend that any earnings will be reinvested in our business and that dividends will not be paid until we have an established revenue stream to support continuing dividends. The proposal to pay future dividends to shareholders will in addition effectively be at the discretion of our board of directors and shareholders after taking into account various factors including our business prospects, cash requirements, financial performance and new product development. In addition, payment of future dividends is subject to certain limitations pursuant to Swiss law or by our articles of association. Accordingly, investors cannot rely on dividend income from our common shares and any returns on an investment in our common shares will likely depend entirely upon any future appreciation in the price of our common shares. Dividends paid on our common shares are subject to Swiss federal withholding tax, except if paid out of reserves from capital contributions ("*Kapitaleinlagen*"). See "Taxation—Swiss Tax Considerations" for a summary of certain Swiss tax consequences regarding dividends distributed to holders of our common shares.

We Are A Swiss Corporation. The Rights Of Our Shareholders May Be Different From The Rights Of Shareholders In Companies Governed By The Laws Of U.S. Jurisdictions.

We are a Swiss corporation. Our corporate affairs are governed by our articles of association and by Swiss law. The rights of our shareholders and the responsibilities of members of our board of directors may be different from the rights and obligations of shareholders and directors of companies governed by the laws of U.S. jurisdictions. In the performance of its duties, our board of directors is required by Swiss law to consider the interests of our Company, our shareholders and our employees with due observation of the principles of reasonableness and fairness. It is possible that the board of directors will consider interests that are different from, or in addition to, your interests as a shareholder. Swiss corporate law limits the ability of our shareholders to challenge resolutions made or other actions taken by our board of directors in court. Our shareholders generally are not permitted to file a suit to reverse a decision or an action taken by our board of directors but are instead only permitted to seek damages for breaches of the duty of care and loyalty. As a matter of Swiss law, shareholder claims against a member of our board of directors for breach of the duty of care and loyalty would have to be brought in Zug, Switzerland, or where the relevant member of our board of directors is domiciled. In addition, under Swiss law, any claims by our shareholders against us must be brought exclusively in Zug, Switzerland.

Our Common Shares Are Issued Under The Laws Of Switzerland, Which May Not Protect Investors In A Similar Fashion Afforded By Incorporation In A U.S. State

We are organized under the laws of Switzerland. However, there can be no assurance that Swiss law will not change in the future or that it will serve to protect investors in a similar fashion afforded under corporate law principles in the U.S., which could adversely affect the rights of investors.

Our Status As A Swiss Corporation May Limit Our Flexibility With Respect To Certain Aspects Of Capital Management And May Cause Us To Be Unable To Make Distributions Without Subjecting Our Shareholders To Swiss Withholding Tax.

Swiss law allows our shareholders to authorize share capital that can be issued by the board of directors without additional shareholder approval. This authorization is limited to 50% of the existing registered share capital and must be

renewed by the shareholders every two years. Additionally, subject to specified exceptions, Swiss law grants preemptive rights to existing shareholders to subscribe to any new issuance of shares. Swiss law also does not provide as much flexibility in the various terms that can attach to different classes of shares as the laws of some other jurisdictions. Swiss law also reserves for

Table of Contents

approval by shareholders certain corporate actions over which a board of directors would have authority in some other jurisdictions. For example, the payment of dividends and the cancellation of treasury shares must be approved by shareholders. These Swiss law requirements relating to our capital management may limit our flexibility, and situations may arise where greater flexibility would have provided substantial benefits to our shareholders.

Under Swiss law, a Swiss corporation may pay dividends only if the corporation has sufficient distributable profits from previous fiscal years, or if the corporation has distributable reserves, each as evidenced by its audited statutory balance sheet, and after allocations to reserves required by Swiss law and our articles of association have been deducted. Freely distributable reserves are generally booked either as "free reserves" or as "capital contributions" (*Kapitaleinlagen*, contributions received from shareholders) in the "reserve from capital contributions." Distributions may be made out of registered share capital—the aggregate par value of a company's registered shares—only by way of a capital reduction. We will not be able to pay dividends or make other distributions to shareholders on a Swiss withholding tax-free basis in excess of our aggregate qualifying contributions and registered share capital unless we increase our share capital or our reserves from capital contributions. We would also be able to pay dividends out of distributable profits or freely distributable reserves, but such dividends would be subject to Swiss withholding taxes. There can be no assurance that we will have sufficient distributable profits, free reserves, reserves from capital contributions or registered share capital to pay a dividend or effect a capital reduction, that our shareholders will approve dividends or capital reductions proposed by us or that we will be able to meet the other legal requirements for dividend payments or distributions as a result of capital reductions.

Generally, Swiss withholding tax of 35% is due on dividends and similar distributions to our shareholders, regardless of the place of residency of the shareholder, unless the distribution is made to shareholders out of (i) a reduction of registered share capital or (ii) assuming certain conditions are met, qualifying capital contribution reserves, as further described under "Taxation—Swiss Tax Considerations—Swiss Federal Withholding Tax". A U.S. holder that qualifies for benefits under the Convention between the United States of America and Switzerland for the Avoidance of Double Taxation with Respect to Taxes on Income, or the U.S.-Swiss Treaty, may apply for a refund of the tax withheld in excess of the 15% treaty rate (or in excess of the 5% reduced treaty rate for qualifying corporate shareholders with at least 10% participation in our voting shares, or for a full refund in the case of qualified pension funds). There can be no assurance that we will have sufficient qualifying capital contribution reserves to pay dividends free from Swiss withholding tax, or that Swiss withholding rules will not be changed in the future. In addition, we cannot provide assurance that the current Swiss law with respect to distributions out of qualifying capital contribution reserves will not be changed or that a change in Swiss law will not adversely affect us or our shareholders, in particular as a result of distributions out of qualifying capital contribution reserves becoming subject to additional corporate law or other restrictions. There are currently ongoing discussions in the Swiss Parliament that may limit the distribution of qualifying capital contributions. In addition, over the long term, the amount of registered share capital available to us for registered share capital reductions or qualifying capital contributions available to us to pay out as distributions is limited. If we are unable to make a distribution through a reduction in par value or out of qualifying capital contributions, we may not be able to make distributions without subjecting our shareholders to Swiss withholding taxes.

Under present Swiss tax laws, repurchases of shares for the purposes of cancellation are treated as a partial liquidation subject to 35% Swiss withholding tax on the difference between the repurchase price and the par value except, since January 1, 2011, to the extent attributable to qualifying capital contributions (*Kapitaleinlagen*) if any, the Swiss withholding becomes due. No partial liquidation treatment applies and no withholding tax is triggered if the shares are not repurchased for cancellation but held by us as treasury shares. However, should we not resell such treasury shares within six years, the withholding tax becomes due at the end of the six year period.

Certain U.S. Shareholders May Be Subject To Adverse U.S. Federal Income Tax Consequences If We Are Classified As A Controlled Foreign Corporation.

Each "Ten Percent Shareholder" (as defined below) in a non-U.S. corporation that is classified as a "controlled foreign corporation," or a CFC, for United States federal income tax purposes generally is required to include in income for U.S. federal tax purposes such Ten Percent Shareholder's pro rata share of the CFC's "Subpart F income" and investment of earnings in U.S. property, even if the CFC has made no distributions to its shareholders. Subpart F income generally includes dividends, interest, rents and royalties, gains from the sale of securities and income from certain transactions with related parties. For tax years beginning after December 31, 2017, the Tax Reform Act (as defined below) expands Subpart F income to include certain global intangible low tax income. In addition, a Ten Percent Shareholder that realizes gain from the sale or exchange of shares in a CFC may be required to classify a portion of such gain as dividend income rather than capital gain. A non-U.S. corporation generally will be classified as a CFC for United States federal income tax purposes if Ten Percent

Shareholders own, directly or indirectly, more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the U.S. Internal Revenue Code of 1986, as amended (the "Code")) who owns or is considered to own 10% or more of the total combined voting power of all classes of stock entitled to vote of such corporation. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain. For tax years beginning after December 31, 2017, the Tax Reform Act (as defined below) expands the definition of a Ten Percent Shareholder to be a United States person (as defined by the Code) who owns or is considered to own 10% or more of the total (1) combined voting power of all classes of stock entitled to vote of such corporation or (2) value of all classes of stock of such corporation. See also "Risk Factor — Comprehensive Tax Reform Legislation Could Adversely Affect Our Business And Financial Condition."

Table of Contents

We believe that certain of our shareholders are Ten Percent Shareholders as of immediately prior to this offering. We have not determined whether we are currently a CFC or whether we may be a CFC following the offering. It is possible, however, that a shareholder treated as a U.S. person for U.S. federal income tax purposes will acquire, directly or indirectly, enough shares to be treated as a Ten Percent Shareholder after application of the constructive ownership rules and, together with any other Ten Percent Shareholders of our Company, cause us to be treated as a CFC for the current tax year or any future tax year. U.S. holders should consult their own tax advisors with respect to the potential adverse U.S. tax consequences of becoming a Ten Percent Shareholder in a CFC. If we are classified as both a CFC and a PFIC, we generally will not be treated as a PFIC with respect to those U.S. holders that meet the definition of a Ten Percent Shareholder during the period in which we are a CFC.

Certain U.S. Shareholders May Suffer Adverse Tax Consequences If We Are Characterized As A Passive Foreign Investment Company.

Generally, if, for any taxable year, at least 75% of our gross income is passive income, or at least 50% of the value of our assets is attributable to assets that produce passive income or are held for the production of passive income, including cash, we would be characterized as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes. For purposes of these tests, passive income includes dividends, interest, and gains from the sale or exchange of investment property and rents and royalties other than rents and royalties which are received from unrelated parties in connection with the active conduct of a trade or business. If we are characterized as a PFIC, U.S. holders of our common shares may suffer adverse tax consequences, including having gains realized on the sale of the common shares treated as ordinary income, rather than capital gain, the loss of the preferential rate applicable to dividends received on the common shares by individuals who are U.S. holders, and having interest charges apply to distributions by us and the proceeds of sales of the common shares. See "Material U.S. Federal Income Tax Considerations to U.S. Holders—Passive Foreign Investment Company Considerations." See also "Risk Factor — Comprehensive Tax Reform Legislation Could Adversely Affect Our Business And Financial Condition."

Our status as a PFIC will depend on the composition of our income and the composition and value of our assets which may be determined in part by reference to the quarterly market value of our common shares, which may be volatile. Our status may also depend, in part, on how, and how quickly, we utilize the cash proceeds from this offering in our business. Our status as a PFIC is a fact-intensive determination made on an annual basis and we cannot provide any assurances regarding our PFIC status for any past, current or future taxable years.

Because it is possible we were a PFIC for the 2016 taxable year, we provided information necessary for our shareholders to make a QEF election with respect to us for the 2016 taxable year. We provided such information on our website (www.crisprtx.com). For the 2016 taxable year, the amount of our ordinary earnings and net capital gain for purposes of the QEF inclusion rules was zero. Although we have not yet determined whether we are a PFIC for the current taxable year, it is possible that we may be a PFIC for the 2017 year as well. We will endeavor to provide to you, for each taxable year that we determine we are a PFIC, a PFIC Annual Information Statement containing information necessary for you to make a QEF election with respect to us.

If we are determined to be a PFIC, a U.S. holder will generally be treated as owning a proportionate amount (by value) of shares owned by us in any of our direct or indirect subsidiaries that are also PFICs, each a lower-tier PFIC, and will be subject to similar adverse rules with respect to distributions from, or dispositions of, such lower-tier PFICs, in each case as if such U.S. holder held such shares directly (even if such U.S. holder does not receive the proceeds of such distributions or dispositions directly). We have not determined whether any of our subsidiaries (including TRACR Hematology Ltd. and CRISPR Therapeutics Ltd.) are or may be lower-tier PFICs for the 2016 taxable year, the current taxable year or future taxable years, and we do not intend to do so. We also do not intend to make available the information necessary for U.S. holders to make a QEF election with respect to any lower-tier PFICs and therefore you should expect that you will not be able to make a QEF election with respect to them. You are urged to consult your own tax advisors regarding our PFIC status and the tax considerations relevant to an investment in a PFIC, including the availability, and advisability, of, and procedure for making, a QEF election with respect to us, and the application of the PFIC rules to any of our subsidiaries.

Comprehensive Tax Reform Legislation Could Adversely Affect Our Business And Financial Condition.

The U.S. government has recently enacted comprehensive tax legislation that includes significant changes to the taxation of business entities, referenced herein as the Tax Reform Act. These changes include, among others, a permanent reduction to the corporate income tax rate. Notwithstanding the reduction in the corporate income tax rate, the overall impact

of this tax reform is uncertain, and our business and financial condition could be adversely affected. The overall impact of the Tax Reform Act on shareholders is uncertain, and this prospectus does not address, other than as expressly addressed herein, the manner in which it may affect purchasers of our common shares. We urge our shareholders to consult with their legal and tax advisors with respect to any such legislation and the potential tax consequences of investing in our common shares.

Table of Contents

U.S. Shareholders May Not Be Able To Obtain Judgments Or Enforce Civil Liabilities Against Us Or Our Executive Officers Or Members Of Our Board Of Directors.

We are organized under the laws of Switzerland and our registered office and domicile is located in Zug, Switzerland. Moreover, certain of our directors and executive officers and a number of directors of each of our subsidiaries are not residents of the United States, and all or a substantial portion of the assets of such persons are located outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon us or upon such persons or to enforce against them judgments obtained in U.S. courts, including judgments in actions predicated upon the civil liability provisions of the federal securities laws of the United States. We have been advised by our Swiss counsel that there is doubt as to the enforceability in Switzerland of original actions, or in actions for enforcement of judgments of U.S. courts, of civil liabilities to the extent solely predicated upon the federal and state securities laws of the United States. Original actions against persons in Switzerland based solely upon the U.S. federal or state securities laws are governed, among other things, by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides that the application of provisions of non-Swiss law by the courts in Switzerland shall be precluded if the result is incompatible with Swiss public policy. Also, mandatory provisions of Swiss law may be applicable regardless of any other law that would otherwise apply.

Switzerland and the United States do not have a treaty providing for reciprocal recognition and enforcement of judgments in civil and commercial matters. The recognition and enforcement of a judgment of the courts of the United States in Switzerland is governed by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides in principle that a judgment rendered by a non-Swiss court may be enforced in Switzerland only if:

- the non-Swiss court had jurisdiction pursuant to the Swiss Federal Act on Private International Law;
- the judgment of such non-Swiss court has become final and non-appealable;
- the judgment does not contravene Swiss public policy;
- the court procedures and the service of documents leading to the judgment were in accordance with the due process of law; and
- no proceeding involving the same position and the same subject matter was first brought in Switzerland, or adjudicated in Switzerland, or was earlier adjudicated in a third state and this decision is recognizable in Switzerland.

Table of Contents

USE OF PROCEEDS

We expect to receive net proceeds of approximately $106.6 million from this offering, after deducting underwriting discounts and estimated offering expenses payable by us, or approximately $122.6 million if the underwriters exercise in full their option to purchase up to an additional 750,000 common shares.

As of September 30, 2017, our cash balance was $253.5 million.

We intend to use the net proceeds from this offering as follows:

- approximately $75.0 million to fund clinical development of CTX001, CTX101 and additional pipeline candidates and platform extensions;
- the remainder, if any, for manufacturing, working capital and general corporate purposes.

However, due to the uncertainties inherent in the product development process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering that may be used for the above purposes. The amount and timing of our actual expenditures will depend upon numerous factors, including the results of our research and development efforts, the timing and success of our ongoing preclinical studies or preclinical studies we may commence in the future and the timing of regulatory submissions. As a result, our management will have broad discretion over the use of the net proceeds from this offering, and investors will be relying on our judgment regarding the application of the net proceeds. In addition, we might decide to postpone or not pursue certain preclinical activities if the net proceeds from this offering and our other sources of cash are less than expected.

We believe opportunities may exist from time to time to expand our current business through acquisitions or in-licenses of complementary companies or technologies. While we have no current agreements, commitments or understandings for any specific acquisitions or in-licenses at this time, we may use a portion of the net proceeds for these purposes.

Pending the use of the proceeds from this offering, we intend to invest the net proceeds in interest-bearing, investment-grade securities, certificates of deposit or direct or guaranteed obligations of the U.S. and Swiss governments.

Table of Contents

DILUTION

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

As of September 30, 2017, we had net tangible book value of approximately $178.6 million, or $4.37 per common share, based upon 40,890,954 common shares outstanding as of that date (which includes 64,227 issued but unvested restricted shares subject to repurchase by us and that are not considered outstanding for accounting purposes until vested and 444,873 treasury shares which are legally outstanding but not considered outstanding for accounting purposes). Historical net tangible book value per share is equal to our total tangible assets, less total liabilities, divided by the number of outstanding common shares. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of common shares in this offering and the net tangible book value per common share immediately after this offering.

After giving effect to the sale of 5,000,000 common shares in this offering at the public offering price of $22.75 per share and after deducting underwriting discounts and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2017 would have been approximately $285.2 million, or approximately $6.21 per common share. This represents an immediate increase in as adjusted net tangible book value of $1.85 per share to our existing shareholders and an immediate dilution of $16.54 per share to investors participating in this offering.

Dilution per share to new investors is determined by subtracting net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this per share dilution (assuming the underwriters do not exercise in full their option to purchase additional shares):

Public offering price per share		$22.75
Historical net tangible book value per share as of September 30, 2017	$4.37	
Increase in net tangible book value per share attributable to new investors	$1.85	
As adjusted net tangible book value per share after this offering		$ 6.21
Dilution per share to new investors		$16.54

The foregoing table and discussion is based on 40,890,954 common shares outstanding as of September 30, 2017, including 64,227 issued but unvested restricted shares subject to repurchase by us and that are not considered outstanding for accounting purposes until vested and 444,873 treasury shares which are legally outstanding but not considered outstanding for accounting purposes, and excludes:

- 5,778,629 of our common shares issuable upon the exercise of options outstanding under our 2015 Stock Option Plan, as of September 30, 2017 at a weighted-average exercise price of $12.36 per common share;
- 5,468,024of our common shares reserved for future issuance under our Amended and Restated 2016 Stock Option Plan, plus any future increases in the number of shares of common stock reserved for issuance under the Amended and Restated 2016 Stock Option Plan pursuant to the evergreen provision of the Amended and Restated 2016 Stock Option Plan; and
- 413,226 common shares reserved for issuance under our ESPP.

Table of Contents

If the underwriters exercise in full their option to purchase up to an additional 750,000 common shares at the public offering price of $22.75 per share, the as adjusted net tangible book value after this offering would be $6.46 per share, representing an increase in the as adjusted net tangible book value of $2.09 per share to existing shareholders and immediate dilution in net tangible book value of $16.29 per share to investors purchasing our common shares in this offering at the public offering price of $22.75.

To the extent that any options are exercised, new options are issued under our equity incentive plans, or we otherwise issue additional common shares in the future (including shares issued in connection with acquisitions), there will be further dilution to new investors.

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

Table of Contents

PRICE RANGE OF COMMON SHARES

Our common shares began trading on the Nasdaq Global Market under the symbol "CRSP" on October 19, 2016. Prior to that time, there was no public market for our common shares. The following table sets forth the high and low sale prices per common share, as reported on the Nasdaq Global Market, for the periods indicated:

	Sales prices	
	High	Low
Year ended December 31, 2016		
Fourth quarter (from October 19, 2016)	$23.97	$13.75
Year ending December 31, 2017		
First quarter	$25.00	$11.63
Second quarter	$22.22	$13.50
Third quarter	$21.32	$15.55
Fourth quarter	$25.00	$16.51
Year Ending December 31, 2018		
First quarter (through January 2, 2018)	$27.39	$24.00

As of December 29, 2017, there were 31 record holders of our common shares. The actual number of shareholders is greater than this number of record holders and includes shareholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

Table of Contents

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Under Swiss law, any dividend must be proposed by our board of directors and approved by our shareholders. In addition, our auditors must confirm that the dividend proposal of our board of directors conforms to Swiss statutory law and our articles of association. A Swiss corporation may pay dividends only if it has sufficient distributable profits brought forward from the previous business years ("*Gewinnvortrag*") or if it has distributable reserves ("*freie Reserven*"), each as evidenced by its audited standalone statutory balance sheet prepared pursuant to Swiss law and after allocations to reserves required by Swiss law and its articles of association have been deducted. Distributable reserves are generally booked either as "free reserves" ("*freie Reserven*") or as "reserve from capital contributions" (*"Kapitaleinlagereserven"*). Distributions out of issued share capital, which is the aggregate nominal value of a corporation's issued shares, may be made only by way of a share capital reduction.

Table of Contents

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman Sachs & Co. LLC, Piper Jaffray & Co. and Barclays Capital Inc. are the representatives of the underwriters.

Underwriters	Number of Shares
Goldman Sachs & Co. LLC	2,000,000
Piper Jaffray & Co.	1,500,000
Barclays Capital Inc.	1,000,000
Guggenheim Securities, LLC	500,000
Total	5,000,000

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

The underwriters have an option to buy up to an additional 750,000 shares from us to cover sales by the underwriters of a greater number of shares than the total number set forth in the table above. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase 750,000 additional shares.

Paid by Us	No Exercise	Full Exercise
Per Share	$ 1.365	$ 1.365
Total	$6,825,000	$7,848,750

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $0.819 per share from the public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

We and certain of our directors and officers and shareholders have agreed with the underwriters, subject to certain exceptions, not to dispose of or hedge any of the common shares or securities convertible into or exchangeable for common shares during the period from the date of this prospectus supplement continuing through the date 90 days after the date of this prospectus supplement, except with the prior written consent of the representatives. This agreement does not apply to any existing employee benefit plans.

The restrictions described in the immediately preceding paragraph do not apply to our directors, executive officers and shareholders with respect to:

- transfers or dispositions (1) as a bona fide gift, (2) to an immediate family member of the undersigned or to a trust formed for the direct or indirect benefit of the undersigned or an immediate family member of the undersigned, (3) by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or trustee of the undersigned or (4) pursuant to a divorce settlement agreement or decree or a qualified domestic relations order; provided that in each case, each recipient agrees to be bound in writing by the same restrictions, such transfers shall not involve a disposition for value and no filing under Section 13 or Section 16(a) of the Exchange Act or other public filing or announcement shall be required or voluntarily made during the restricted period;

- transactions relating to common shares acquired in open market transactions after the completion of the offering, provided that with respect to such open market transactions, no filing under Section 13 or Section 16(a) of the Exchange Act or other public filing or announcement shall be required or voluntarily made during the restricted period;

Table of Contents

- exercise of options or warrants to purchase common shares or the receipt of common shares upon the vesting of restricted common share awards and any related transfer of common shares to us in connection therewith (x) deemed to occur upon the "cashless" or "net" exercise of such options or warrants or (y) for the purpose of paying the exercise price of such options or warrants or for paying taxes due as a result of the exercise of such options or warrants, the vesting of such options, warrants or common share awards, or as a result of the vesting of such common shares, provided that all common shares received upon such exercise, vesting or transfer remain subject to the restrictions on transfer described herein and provided that any public filing or announcement required or voluntarily made during the restricted period in connection with such transfer shall clearly indicate that such transfer was made pursuant to the circumstances described above;
- transfers of common shares to us pursuant to agreements under which we have the option to repurchase such common shares, provided that no filing under Section 13 or Section 16(a) of the Exchange Act or other public filing or announcement shall be required or voluntarily made during the restricted period;
- transfers of common shares to any affiliate (as defined in Rule 405 of the Securities Act of 1933, as amended), limited partners, general partners, limited liability company members or shareholders of the undersigned, or if the undersigned is a corporation to any wholly owned subsidiary of such corporation, provided that in each case, the recipient agrees to be bound in writing by the same restrictions, such transfers shall not involve a disposition for value and no filing under Section 13 or Section 16(a) of the Exchange Act or other public filing or announcement shall be required or voluntarily made during the restricted period;
- the establishment of a trading plan by an officer or director of us pursuant to Rule 10b5-1 under the Exchange Act for the transfer of common shares, provided that such plan does not provide for the transfer of common shares during the restricted period and no filing under Section 13 or Section 16(a) of the Exchange Act or other public filing or announcement shall be required or voluntarily made during the restricted period; or
- transfers, sales, tenders or other dispositions of common shares pursuant to a bona-fide third-party tender offer, merger, amalgamation, consolidation or other similar transaction made to or involving all holders of the common shares pursuant to a change of control of the ownership of us, provided that such transaction is approved by our board of directors, and if such transaction is not completed, any common shares subject to restrictions described above remain subject to the restrictions for the restricted period.

In addition, the restrictions described above do not apply to us with respect to:

- the common shares to be sold by us in this offering;
- the issuance and sale by us of common shares pursuant to any employee stock option plan, stock ownership plan or dividend reinvestment plan in effect on the date of this offering; and
- the issuance by us of common shares or any security convertible into or exercisable for common shares in connection with any joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements or in connection with the acquisition by us or our subsidiaries of not less than a majority or controlling portion of the securities, business, property or other assets of another person or entity or pursuant to an employee benefit plan assumed by us in connection with such acquisition, provided that the aggregate number of common shares issued does not exceed 5% of the common shares issued and outstanding immediately following this offering.

In connection with the offering, the underwriters may purchase and sell common shares in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short position that is not greater than the amount of additional shares for which the underwriters' option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover 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 additional shares pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such 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

Table of Contents

downward pressure on the price of the common shares in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common shares made by the underwriters in the open market prior to the completion of the offering.

In connection with the offering, the underwriters and selling group members may engage in passive market making transactions in the common shares on the Nasdaq Global Market in accordance with Rule 103 of Regulation M under the Exchange Act during the period before the commencement of offers or sales of common shares and extending through the completion of distribution. A passive market maker must display its bids at a price not in excess of the highest independent bid of the security. However, if all independent bids are lowered below the passive market maker's bid that bid must be lowered when specified purchase limits are exceeded.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of our common shares, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common shares. As a result, the price of the common shares may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on Nasdaq Global Market, in the over-the-counter market or otherwise.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. In connection with those derivatives, the third parties may sell securities covered by this prospectus, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter or will be identified in a post-effective amendment.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relative Member State") an offer to the public of our common shares may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of our common shares may be made at any time under the following exemptions under the Prospectus Directive:

- To any legal entity which is a qualified investor as defined in the Prospectus Directive;
- To fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the representatives for any such offer; or
- In any other circumstances falling within Article 3(2) of the Prospectus Directive;

provided that no such offer of our common shares shall result in a requirement for the publication by us or any Brazilian placement agent of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to public" in relation to our common shares 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 our common shares to be offered so as to enable an investor to decide to purchase common shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (as amended), including by Directive 2010/73/EU and includes any relevant implementing measure in the Relevant Member State.

This European Economic Area selling restriction is in addition to any other selling restrictions set out below.

United Kingdom

In the United Kingdom, this prospectus is only addressed to and directed as qualified investors who are (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order); or (ii) high net worth entities and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). Any investment or investment activity to which this prospectus relates is available only to relevant persons and will only be engaged with relevant persons. Any person who is not a relevant person should not act or relay on this prospectus or any of its contents.

Table of Contents

Canada

The securities may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions, and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption form, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this offering memorandum (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) ("Companies (Winding Up and Miscellaneous Provisions) Ordinance") or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) ("Securities and Futures Ordinance"), or (ii) to "professional investors" as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued 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 in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA")) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, 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, in each case subject to conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in 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, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation's securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore ("Regulation 32")

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S$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), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

Table of Contents

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended), or the FIEA. The securities may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

Switzerland

The common shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or the SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document 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 document nor any other offering or marketing material relating to the common shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland. Neither this document nor any other offering or marketing material relating to this offering, us or the common shares has been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares 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 shares.

We estimate that our share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately $360,000. We have agreed to reimburse the underwriters for expenses, in an amount up to $25,000, relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc. and the qualification of our common shares under state securities laws.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to us and to persons and entities with relationships with us, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively traded securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to our assets, securities and/or instruments (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with us. The underwriters and 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 assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Table of Contents

TAXATION

The following summary does not purport to address all tax consequences of this offering, the acquisition, the ownership and sale or other disposition of our common shares (such shares for the purposes of this "Taxation" section, "Shares") and does not take into account the specific circumstances of any particular investor. This summary is based on the tax laws, regulations and regulatory practices of Switzerland and the United States as in effect on the date hereof, which are subject to change (or subject to changes in interpretation), possibly with retroactive effect.

Current and prospective shareholders are advised to consult their own tax advisers in light of their particular circumstances as to the Swiss or U.S. tax laws, regulations and regulatory practices that could be relevant for them in connection with this offering, the acquiring, owning and selling or otherwise disposing of Shares and receiving dividends and similar cash or in-kind distributions on Shares (including dividends on liquidation proceeds and stock dividends) or distributions on Shares based upon a capital reduction (Kapitalherabsetzung durch Nennwertreduktion) or reserves paid out of capital contributions (Kapitaleinlagen) and the consequences thereof under the tax laws, regulations and regulatory practices of Switzerland and/or the United States.

Swiss Tax Considerations

Swiss Federal, Cantonal And Communal Individual Income Tax And Corporate Income Tax

Non-Resident Shareholders

Except as discussed in the sections titled "—*Swiss Federal Withholding Tax,*" shareholders who are not resident in Switzerland for tax purposes, and who, during the relevant taxation year, have not engaged in a trade or business carried on through a permanent establishment situated in Switzerland for tax purposes (all such shareholders for purposes of this section, "Non-Resident Shareholders"), will not be subject to any Swiss federal, cantonal and communal income tax on dividends and similar cash or in-kind distributions on Shares (including dividends on liquidation proceeds and stock dividends) (such dividends for the purposes of this, "Dividends"), distributions based upon a capital reduction (*Kapitalherabsetzung durch Nennwertreduktion*) and reserves paid out of capital contributions (*Kapitaleinlagen*) on Shares, or capital gains realized on the sale or other disposition of Shares.

Resident Private Shareholders

Swiss resident individuals who hold their Shares as private assets are required to include Dividends, but not distributions based upon a capital reduction (*Kapitalherabsetzung durch Nennwertreduktion*) and reserves paid out of capital contributions (*Kapitaleinlagen*), in their personal income tax return and are subject to Swiss federal, cantonal and communal income tax on any net taxable income for the relevant taxation period, including the Dividends, but not the distributions based upon a capital reduction (*Kapitalherabsetzung durch Nennwertreduktion*) and reserves paid out of capital contributions (*Kapitaleinlagen*). Capital gains resulting from the sale or other disposition of Shares are generally not subject to Swiss federal, cantonal and communal income tax, and conversely, capital losses are not tax-deductible for Resident Private Shareholders (the shareholders referred to in this paragraph for the purposes of this section, "Resident Private Shareholders"). See "—Domestic Commercial Shareholders" below for a summary of the taxation treatment applicable to Swiss resident individuals, who, for income tax purposes, are classified as "professional securities dealers".

Domestic Commercial Shareholders

Corporate and individual shareholders who are resident in Switzerland for tax purposes, and corporate and individual shareholders who are not resident in Switzerland, and who, in each case, hold their Shares as part of a trade or business carried on in Switzerland, in the case of corporate and individual shareholders not resident in Switzerland, through a permanent establishment situated, for tax purposes, in Switzerland, are required to recognize Dividends, distributions based upon a capital reduction (*Kapitalherabsetzung durch Nennwertreduktion*) and reserves paid out of capital contributions (*Kapitaleinlagen*) received on Shares and capital gains or losses realized on the sale or other disposition of Shares in their income statement for the relevant taxation period and are subject to Swiss federal, cantonal and communal individual or corporate income tax, as the case may be, on any net taxable earnings for such taxation period. The same taxation treatment also applies to Swiss-resident private individuals who, for income tax purposes, are classified as "professional securities dealers" for reasons of, *inter alia*, frequent dealing, or leveraged investments, in shares and other securities (the shareholders referred to in this paragraph for purposes of this section, "Domestic Commercial Shareholders"). Domestic Commercial

Shareholders who are corporate taxpayers may be eligible for dividend relief (*Beteiligungsabzug*) in respect of Dividends and distributions based upon a capital reduction (*Kapitalherabsetzung durch Nennwertreduktion*) and reserves paid out of capital contributions (*Kapitaleinlagen*) if the Shares held by them as part of a Swiss business have an aggregate market value of at least CHF 1 million.

Table of Contents

Swiss Cantonal and Communal Private Wealth Tax and Capital Taxes

Non-Resident Shareholders

Non-Resident Shareholders are not subject to Swiss cantonal and communal private wealth tax or capital tax.

Resident Private Shareholders and Domestic Commercial Shareholders

Resident Private Shareholders and Domestic Commercial Shareholders who are individuals are required to report their Shares as part of private wealth or their Swiss business assets, as the case may be, and will be subject to Swiss cantonal and communal private wealth tax on any net taxable wealth (including Shares), in the case of Domestic Commercial Shareholders to the extent the aggregate taxable wealth is allocable to Switzerland. Domestic Commercial Shareholders who are corporate taxpayers are subject to Swiss cantonal and communal capital tax on taxable capital to the extent the aggregate taxable capital is allocable to Switzerland.

Swiss Federal Withholding Tax

Dividends that we pay on the Shares are subject to Swiss federal withholding tax *(Verrechnungssteuer)* at a rate of 35% on the gross amount of the Dividend. We are required to withhold the Swiss federal withholding tax from the Dividend and remit it to the Swiss Federal Tax Administration. Distributions based upon a capital reduction *(Kapitalherabsetzung durch Nennwertreduktion)* and reserves paid out of capital contributions *(Kapitaleinlagen)* are not subject to Swiss federal withholding tax.

The Swiss federal withholding tax on a Dividend will be refundable in full to a Resident Private Shareholder and to a Domestic Commercial Shareholder to the extent the Shares are allocable to Switzerland, who, in each case, *inter alia,* as a condition to a refund, duly reports the Dividend in his individual income tax return as income or recognizes the Dividend in his income statement as earnings, as applicable.

A Non-Resident Shareholder may be entitled to a full or partial refund of the Swiss federal withholding tax on a Dividend if the country of his or her residence for tax purposes has entered into a bilateral treaty for the avoidance of double taxation with Switzerland and the conditions of such treaty are met. Such shareholders should be aware that the procedures for claiming treaty benefits (and the time required for obtaining a refund) might differ from country to country.

For example, a shareholder who is a resident of the U.S. for the purposes of the Convention between the U.S. and Switzerland for the Avoidance of Double Taxation with Respect to Taxes or Income, is eligible for a refund of the amount of the withholding tax in excess of the 15% treaty rate, or in excess of the 5% reduced treaty rate for qualifying corporate shareholders with at least 10% participation in our voting stock, or for a full refund in the case of qualified pension funds, provided, in each case, such shareholder: (i) qualifies for benefits under the treaty (ii) qualifies as beneficial owner of the Dividends; and (iii) does not conduct business through a permanent establishment or fixed base in Switzerland to which the Shares are attributable. The applicable refund request form may be filed with the Swiss Federal Tax Administration following receipt of the Dividend and the relevant deduction certificate, however no later than 31 December of the third year following the calendar year in which the Dividend was payable.

Swiss Federal Stamp Taxes

We will be subject to and pay to the Swiss Federal Tax Administration a 1% Swiss federal issuance stamp tax *(Emissionsabgabe)* on the consideration received for the issuance of the Shares less certain costs incurred in connection with the issuance.

The issuance of the Shares to the initial shareholders at the offering price is not subject to Swiss federal securities turnover tax *(Umsatzabgabe).*

Any subsequent dealings in the Shares, where a bank or another securities dealer in Switzerland, as defined in the Swiss Federal Stamp Tax Act, acts as an intermediary, or is a party, to the transaction, are, subject to certain exemptions provided for in the Swiss Federal Stamp Tax Act, subject to Swiss securities turnover tax at an aggregate tax rate of 0.15% of the consideration paid for such Shares.

THE DISCUSSION ABOVE IS A SUMMARY OF MATERIAL SWISS TAX CONSIDERATIONS. IT DOES NOT COVER ALL TAX MATTERS THAT MAY BE OF IMPORTANCE TO A PARTICULAR PROSPECTIVE INVESTOR. EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES TO IT OF AN INVESTMENT IN THE SHARES IN LIGHT OF THE INVESTOR'S OWN CIRCUMSTANCES.

Table of Contents

Material U.S. Federal Income Tax Considerations to U.S. Holders

The following is a summary of material U.S. federal income tax considerations relating to the acquisition, ownership and disposition of the common shares by a U.S. holder (as defined below). This summary addresses only the U.S. federal income tax considerations for U.S. holders that are initial purchasers of the common shares pursuant to this offering and that will hold such common shares as capital assets (generally, property held for investment) for U.S. federal income tax purposes and does not apply to any shares acquired in the concurrent private placement. This summary does not address all U.S. federal income tax matters that may be relevant to a particular U.S. holder. This summary does not address tax considerations applicable to a holder of common shares that may be subject to special tax rules including, without limitation, the following:

- banks, financial institutions or insurance companies;
- brokers, dealers or traders in securities, currencies, commodities, or notional principal contracts;
- tax-exempt entities or organizations, including an "individual retirement account" or "Roth IRA" as defined in Section 408 or 408A of the Code (as defined below), respectively;
- real estate investment trusts, regulated investment companies or grantor trusts;
- persons that hold the common shares as part of a "hedging," "integrated" or "conversion" transaction or as a position in a "straddle" for U.S. federal income tax purposes;
- partnerships (including entities classified as partnerships for U.S. federal income tax purposes) or other pass-through entities, or persons that will hold the common shares through such an entity;
- certain former citizens or long term residents of the United States;
- holders that own directly, indirectly, or through attribution 10% or more of the voting power or value of the common shares; and
- holders that have a "functional currency" for U.S. federal income tax purposes other than the U.S. dollar.

Further, this summary does not address the U.S. federal estate, gift, or alternative minimum tax considerations, or any U.S. state, local, or non-U.S. tax considerations of the acquisition, ownership and disposition of the common shares.

This description is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code; existing, proposed and temporary U.S. Treasury Regulations promulgated thereunder, administrative and judicial interpretations thereof; and the income tax treaty between the United States and the Swiss Confederation in each case as in effect and available on the date hereof. All the foregoing is subject to change, which change could apply retroactively, and to differing interpretations, all of which could affect the tax considerations described below. As discussed above under "Risk Factors", the U.S. government recently enacted the Tax Reform Act, the overall impact of which is currently uncertain. The overall impact of the Tax Reform Act on shareholders is uncertain, and this prospectus does not address, other than as expressly addressed herein, the manner in which it may affect purchasers of our common shares. Holders should consult with their advisors regarding the impact of the Tax Reform Act on the tax consequences of acquiring, owning, and disposing of the common shares in their particular circumstances. We have not received nor do we expect to seek a ruling from the U.S. Internal Revenue Service, or the IRS, regarding any matter discussed herein. There can be no assurances that the IRS will not take a contrary or different position concerning the tax consequences of the acquisition, ownership and disposition of the common shares or that such a position would not be sustained. Holders should consult their own tax advisers concerning the U.S. federal, state, local and non-U.S. tax consequences of acquiring, owning, and disposing of the common shares in their particular circumstances.

For the purposes of this summary, a "U.S. holder" is a beneficial owner of common shares that is (or is treated as), for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity that is treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or

- a trust, if a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of the substantial decisions of such trust or has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a United States person.

Table of Contents

If a partnership (or any other entity treated as a partnership for U.S. federal income tax purposes) holds common shares, the U.S. federal income tax consequences relating to an investment in the common shares will depend in part upon the status of the partner and the activities of the partnership. Such a partner or partnership should consult its tax advisor regarding the U.S. federal income tax considerations of acquiring, owning and disposing of the common shares in its particular circumstances.

As indicated below, this discussion is subject to U.S. federal income tax rules applicable to a "passive foreign investment company," or a PFIC. As discussed below under "Passive Foreign Investment Company Considerations," we believe we may have been a PFIC with respect to the 2016 taxable year and it is possible we may be a PFIC for our current taxable year as well. In addition, it is possible that we will be a CFC for a taxable year following the year of this offering, and if we are a CFC, this discussion assumes that a "U.S. holder" does not include a holder that is a United States person (within the meaning of the Code) who owns or is considered to own (i) 10% or more of the total combined voting power of all classes of our stock entitled to vote or (ii) 10% or more of the total value of all classes of stock of such corporation.

Persons considering an investment in the common shares should consult their own tax advisors as to the particular tax consequences applicable to them relating to the acquisition, ownership and disposition of the common shares, including the applicability of U.S. federal, state and local tax laws and non-U.S. tax laws.

Distributions

Although we do not currently plan to pay dividends, and subject to the discussion under "Passive Foreign Investment Company Considerations" below, the gross amount of any distribution (before reduction for any amounts withheld in respect of Swiss withholding tax, if any) actually or constructively received by a U.S. holder with respect to common shares will be taxable to the U.S. holder as a dividend to the extent of the U.S. holder's pro rata share of our current and accumulated earnings and profits as determined under U.S. federal income tax principles. Distributions in excess of earnings and profits will be non-taxable to the U.S. holder to the extent of, and will be applied against and reduce, the U.S. holder's adjusted tax basis in the common shares. Distributions in excess of earnings and profits and such adjusted tax basis will generally be taxable to the U.S. holder as either long-term or short-term capital gain depending upon whether the U.S. holder has held the common shares for more than one year as of the time such distribution is received. However, since we do not calculate our earnings and profits under U.S. federal income tax principles, it is expected that any distribution will be reported as a dividend, even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above. Non-corporate U.S. holders may qualify for the preferential rates of taxation with respect to dividends on common shares applicable to long-term capital gains (i.e., gains from the sale of capital assets held for more than one year) applicable to qualified dividend income (as discussed below) if we are a "qualified foreign corporation" and certain other requirements (discussed below) are met. A non-United States corporation (other than a corporation that is classified as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year) generally will be considered to be a qualified foreign corporation (a) if it is eligible for the benefits of a comprehensive tax treaty with the United States which the Secretary of Treasury of the United States determines is satisfactory for purposes of this provision and which includes an exchange of information provision, or (b) with respect to any dividend it pays on shares of stock which are readily tradable on an established securities market in the United States. We expect that the common shares will be listed on Nasdaq, which is an established securities market in the United States, and we expect the common shares to be readily tradable on Nasdaq. However, there can be no assurance that the common shares will be considered readily tradable on an established securities market in the United States in later years. As we are incorporated under the laws of the Swiss Confederation, we believe that we qualify as a resident of Switzerland for purposes of, and is eligible for the benefits of, The Convention between the United States of America and the Swiss Confederation for the Avoidance of Double Taxation with Respect to Taxes on Income, signed on October 2, 1996, or the U.S.-Swiss Tax Treaty, although there can be no assurance in this regard. Further, the IRS has determined that the U.S.-Swiss Tax Treaty is satisfactory for purposes of the qualified dividend rules and that it includes an exchange-of-information program. Therefore, subject to the discussion under "Passive Foreign Investment Company Considerations" below, such dividends will generally be "qualified dividend income" in the hands of individual U.S. holders, provided that a holding period requirement (more than 60 days of ownership, without protection from the risk of loss, during the 121-day period beginning 60 days before the ex-dividend date) and certain other requirements are met. The dividends will not be eligible for the dividends-received deduction generally allowed to corporate U.S. holders.

A U.S. holder generally may claim the amount of any Swiss withholding tax as either a deduction from gross income or a credit against U.S. federal income tax liability. However, the foreign tax credit is subject to numerous complex limitations that must be determined and applied on an individual basis. Generally, the credit cannot exceed the proportionate

share of a U.S. holder's U.S. federal income tax liability that such U.S. holder's taxable income bears to such U.S. holder's worldwide taxable income. In applying this limitation, a U.S. holder's various items of income and deduction must be classified, under complex rules, as either "foreign source" or "U.S. source." In addition, this limitation is calculated separately with respect to specific categories of income. The amount of a distribution with respect to the common shares that is treated as a "dividend" may be lower for U.S. federal income tax purposes than it is for Swiss income tax purposes, potentially resulting in a reduced foreign tax credit for the U.S. holder. Each U.S. holder should consult its own tax advisors regarding the foreign tax credit rules.

Table of Contents

While we do not currently plan to pay any dividends, the currency of any dividends that we may pay is subject to future determination. If we pay any such dividends in a currency other than U.S. dollars (a "foreign currency"), the amount of a distribution paid to a U.S. holder in a foreign currency will be the U.S. dollar value of the foreign currency calculated by reference to the spot exchange rate on the day the U.S. holder receives the distribution, regardless of whether the foreign currency is converted into U.S. dollars at that time. Any foreign currency gain or loss a U.S. holder realizes on a subsequent conversion of foreign currency into U.S. dollars will be U.S. source ordinary income or loss. If dividends received in a foreign currency are converted into U.S. dollars on the day they are received, a U.S. holder should not be required to recognize foreign currency gain or loss in respect of the dividend.

Sale, Exchange or Other Taxable Disposition of the Common Shares

A U.S. holder will generally recognize gain or loss for U.S. federal income tax purposes upon the sale, exchange or other taxable disposition of common shares in an amount equal to the difference between the U.S. dollar value of the amount realized from such sale or exchange and the U.S. holder's tax basis for those common shares. Subject to the discussion under "Passive Foreign Investment Company Considerations" below, this gain or loss will generally be a capital gain or loss. The adjusted tax basis in the common shares generally will be equal to the U.S. holder's U.S. dollar purchase price of such common shares. Capital gain from the sale, exchange or other taxable disposition of common shares of a non-corporate U.S. holder is generally eligible for a preferential rate of taxation applicable to capital gains, if the non-corporate U.S. holder's holding period determined at the time of such sale, exchange or other taxable disposition for such common shares exceeds one year (i.e., such gain is long-term taxable gain). The deductibility of capital losses for U.S. federal income tax purposes is subject to limitations under the Code. Any such gain or loss that a U.S. holder recognizes generally will be treated as U.S. source income or loss for foreign tax credit limitation purposes.

Medicare Tax

Certain U.S. holders that are individuals, estates or trusts are subject to a 3.8% tax on all or a portion of their "net investment income," which may include all or a portion of their dividend income and net gains from the disposition of common shares. Each U.S. holder that is an individual, estate or trust is urged to consult its tax advisors regarding the applicability of the Medicare tax to its income and gains in respect of its investment in the common shares.

Passive Foreign Investment Company Considerations

If we are classified as a passive foreign investment company in any taxable year, a U.S. holder would be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

A corporation organized outside the United States generally will be classified as a PFIC for U.S. federal income tax purposes in any taxable year in which, after applying certain look-through rules with respect to the income and assets of its subsidiaries, either: (i) at least 75% of its gross income is "passive income," the Income Test or (ii) at least 50% of the average quarterly value of its total gross assets (which, assuming we were a non-publicly traded CFC for the year being tested, must be measured by the adjusted tax basis of our assets or, if we were a publicly traded CFC or not a CFC for such year, the total value of our assets may be determined in part by reference to the quarterly market value of our common shares, which may be volatile) is attributable to assets that produce "passive income" or are held for the production of "passive income," the Asset Test.

Passive income for this purpose generally includes dividends, interest, royalties, rents, gains from commodities and securities transactions, the excess of gains over losses from the disposition of assets which produce passive income, and includes amounts derived by reason of the temporary investment of funds raised in offerings of the common shares. If a non-U.S. corporation owns directly or indirectly at least 25% by value of the stock of another corporation, the non-U.S. corporation is treated for purposes of the PFIC tests as owning its proportionate share of the assets of the other corporation and as receiving directly its proportionate share of the other corporation's income. If we are classified as a PFIC in any year with respect to which a U.S. holder owns the common shares, absent the "deemed sale" election described below, we will continue to be treated as a PFIC with respect to such U.S. holder in all succeeding years during which the U.S. holder owns the common shares, regardless of whether we continue to meet the tests described above.

Whether we are a PFIC for any taxable year will depend on the composition of our income and the projected composition and estimated fair market values of our assets in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will not be considered a PFIC in any taxable year. In addition, the composition of our income and assets will be affected by how, and how quickly, we use the cash proceeds from this offering in our business.

Table of Contents

Because it is possible we were a PFIC for the 2016 taxable year, we provided information necessary for our shareholders to make a QEF election with respect to us for the 2016 taxable year on our website (www.crisprtx.com). For the 2016 taxable year, the amount of our ordinary earnings and net capital gain for purposes of the QEF inclusion rules was zero. Although we have not yet determined our PFIC status for the current taxable year, it is possible that we may be a PFIC for our current taxable year and future taxable years. Our status as a PFIC is a fact-intensive determination made on an annual basis and we cannot provide any assurances regarding our PFIC status for any past, current or future taxable years.

If we are a PFIC, and you are a U.S. holder, then unless you make one of the elections described below, a special tax regime will apply to both (a) any "excess distribution" by us to you (generally, your ratable portion of distributions in any year which are greater than 125% of the average annual distribution received by you in the shorter of the three preceding years or your holding period for the common shares) and (b) any gain realized on the sale or other disposition, including a pledge, of the common shares. Under this regime, any excess distribution and realized gain will be treated as ordinary income and will be subject to tax as if (a) the excess distribution or gain had been realized ratably over your holding period, (b) the amount deemed realized in each year had been subject to tax in each year of that holding period at the highest marginal rate for such year (other than income allocated to the current period or any taxable period before we became a PFIC, which would be subject to tax at the U.S. holder's regular ordinary income rate for the current year and would not be subject to the interest charge discussed below), and (c) the interest charge generally applicable to underpayments of tax had been imposed on the taxes deemed to have been payable in those years. In addition, dividend distributions made to you will not qualify for the lower rates of taxation applicable to long-term capital gains discussed above under "Distributions."

If we are a PFIC for any year during which a U.S. holder holds the common shares, we must generally continue to be treated as a PFIC by that U.S. holder for all succeeding years during which the U.S. holder holds the common shares, unless we cease to meet the requirements for PFIC status and the U.S. holder makes a "deemed sale" election with respect to the common shares. If such election is made, the U.S. holder will be deemed to have sold the common shares it holds at their fair market value on the last day of the last taxable year in which we qualified as a PFIC, and any gain from such deemed sale would be subject to the consequences described above. After the deemed sale election, the U.S. holder's common shares with respect to which the deemed sale election was made will not be treated as shares in a PFIC unless we subsequently become a PFIC.

Certain elections exist that may alleviate some of the adverse consequences of PFIC status and would result in an alternative treatment (such as mark-to-market treatment) of the common shares. If a U.S. holder makes the mark-to-market election, the U.S. holder generally will recognize as ordinary income any excess of the fair market value of the common shares at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the common shares over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. holder makes the election, the U.S. holder's tax basis in the common shares will be adjusted to reflect these income or loss amounts. Any gain recognized on the sale or other disposition of common shares in a year when we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). The mark-to-market election is available only if we are a PFIC and the common shares are "regularly traded" on a "qualified exchange." The common shares will be treated as "regularly traded" in any calendar year in which more than a de minimis quantity of the common shares are traded on a qualified exchange on at least 15 days during each calendar quarter (subject to the rule that trades that have as one of their principal purposes the meeting of the trading requirement as disregarded). Nasdaq is a qualified exchange for this purpose and, consequently, if the common shares are regularly traded, the mark-to-market election will be available to a U.S. holder.

Alternatively, you may avoid the general tax treatment for PFICs described above by electing to treat us as a "qualified electing fund" under Section 1295 of the Code, or QEF, for each of the taxable years during your holding period that we are a PFIC. If a QEF election is not in effect for the first taxable year in your holding period in which we are a PFIC, a QEF election generally can only be made if you elect to make an applicable deemed sale or deemed dividend election on the first day of your taxable year in which the PFIC becomes a QEF pursuant to the QEF election. The deemed gain or deemed dividend recognized with respect to such an election would be subject to the general tax treatment of PFICs discussed above. We intend to determine our PFIC status at the end of each taxable year and to satisfy any applicable record keeping and reporting requirements that apply to a QEF, and will endeavor to provide to you, for each taxable year that we determine we are a PFIC, a PFIC Annual Information Statement containing information necessary for you to make a QEF election with respect to us. We may elect to provide such information on our website..

Table of Contents

If you make a QEF election with respect to a PFIC, you will be taxed currently on your pro rata share of the PFIC's ordinary earnings and net capital gain (at ordinary income and capital gain rates, respectively) for each taxable year that the entity is a PFIC, even if no distributions were received. Any distributions we make out of our earnings and profits that were previously included in your income under the QEF election would not be taxable to you. Your tax basis in your common shares would be increased by an amount equal to any income included under the QEF election and decreased by any amount distributed on the common shares that is not included in your income. In addition, you will recognize capital gain or loss on the disposition of your common shares in an amount equal to the difference between the amount realized and your adjusted tax basis in the common shares, each as determined in U.S. dollars. Once made, a QEF election remains in effect unless invalidated or terminated by the IRS or revoked by the shareholder. A QEF election can be revoked only with the consent of the IRS. You will not be currently taxed on the ordinary income and net capital gain of a PFIC with respect to which a QEF election was made for any taxable year of the non-U.S. corporation that such corporation does not satisfy the PFIC Income Test or Asset Test.

You are urged to consult your own tax advisors regarding the availability of, and procedure for making, any deemed gain, deemed dividend or QEF election.

If we are determined to be a PFIC, a U.S. holder will generally be treated as owning a proportionate amount (by value) of shares owned by us in any direct or indirect subsidiaries that are also PFICs, each a lower-tier PFIC, and will be subject to similar adverse rules with respect to distributions from, or dispositions of, such lower-tier PFICs, in each case as if such U.S. holder held such shares directly (even if such U.S. holder does not receive the proceeds of such distributions or dispositions directly). We have not determined whether any of our subsidiaries (including TRACR Hematology Ltd. and CRISPR Therapeutics Ltd.) are or may be lower-tier PFICs for the 2016 taxable year, the current taxable year or future taxable years, and we do not intend to do so. We also do not intend to make available the information necessary for U.S. holders to make a QEF election with respect to any lower-tier PFICs and therefore you should expect that you will not be able to make a QEF election with respect to them. The mark-to-market election is not permitted for the shares of any of our subsidiaries that are also classified as PFICs. U.S. holders are urged to consult their tax advisors about the application of the PFIC rules to any of our subsidiaries.

If a U.S. holder owns common shares during any taxable year in which we are a PFIC, the U.S. holder generally will be required to file an IRS Form 8621 (Information Return by a Shareholder of a Passive Foreign Investment Company or Qualified Electing Fund) with respect to us and any lower-tier PFIC such U.S. holder is treated as owning pursuant to the rules described above, generally with the U.S. holder's federal income tax return for that year.

The U.S. federal income tax rules relating to PFICs are complex. Prospective U.S. investors are urged to consult their own tax advisers with respect to the acquisition, ownership and disposition of the common shares, the consequences to them of an investment in a PFIC, any elections available with respect to the common shares (including the unavailability of the market-to-market and QEF elections with respect to any lower-tier PFICs) and the IRS information reporting obligations applicable in connection with the acquisition, ownership and disposition of the common shares.

Backup Withholding and Information Reporting

U.S. holders generally will be subject to information reporting requirements with respect to dividends on the common shares and on the proceeds from the sale, exchange or disposition of common shares that are paid within the United States or through U.S.-related financial intermediaries (and certain subsidiaries thereof), unless the U.S. holder is an "exempt recipient." In addition, U.S. holders may be subject to backup withholding on such payments, unless the U.S. holder provides a taxpayer identification number and a duly executed IRS Form W-9 or otherwise establishes an exemption. Backup withholding is not an additional tax, and the amount of any backup withholding will be allowed as a credit against a U.S. holder's U.S. federal income tax liability and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

Foreign Asset Reporting

Certain U.S. holders who are individuals are required to report information relating to an interest in the common shares, subject to certain exceptions (including an exception for shares held in accounts maintained by U.S. financial institutions) by filing IRS Form 8938 (Statement of Specified Foreign Financial Assets) with their federal income tax return.

U.S. holders are urged to consult their tax advisors regarding their information reporting obligations, if any, with respect to their ownership and disposition of the common shares.

THE DISCUSSION ABOVE IS A SUMMARY OF MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS TO U.S. HOLDERS. IT DOES NOT COVER ALL TAX MATTERS THAT MAY BE OF IMPORTANCE TO A PARTICULAR PROSPECTIVE INVESTOR. EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES TO IT OF AN INVESTMENT IN THE SHARES IN LIGHT OF THE INVESTOR'S OWN CIRCUMSTANCES.

Table of Contents

LEGAL MATTERS

The validity of the common shares and certain other matters of Swiss law will be passed upon for us by Vischer AG, Zurich, Switzerland. Certain matters of U.S. federal and Delaware state law will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts, and for the underwriters by Ropes & Gray LLP, Boston, Massachusetts.

EXPERTS

The consolidated financial statements of CRISPR Therapeutics AG appearing in CRISPR Therapeutics AG's Annual Report on Form 10-K for the year ended December 31, 2016 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of said firm as experts in auditing and accounting.

Table of Contents

PROSPECTUS

CRISPR THERAPEUTICS AG

$300,000,000

Common Shares
Debt Securities
Warrants
Units
Subscription Rights

From time to time, we may offer up to $300,000,000 of any combination of the securities described in this prospectus in one or more offerings. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable anti-dilution provisions.

This prospectus provides a general description of the securities we may offer. Each time we offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should carefully read this prospectus and the applicable prospectus supplement, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

This prospectus may not be used to consummate a sale of any securities unless accompanied by a prospectus supplement.

Our common shares trade on the NASDAQ Global Market under the symbol "CRSP." On November 8, 2017, the last reported sale price of our common shares was $17.94 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on the NASDAQ Global Market or any securities market or other exchange of the securities, if any, covered by the prospectus supplement.

We will sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts or over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and under similar headings in the other documents that are incorporated by reference into this prospectus as described on page 3 of this prospectus.

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

The date of this prospectus is December 4, 2017.

Table of Contents

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS	1
CRISPR THERAPEUTICS AG	2
RISK FACTORS	3
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	4
RATIO OF EARNINGS TO FIXED CHARGES	5
USE OF PROCEEDS	6
COMPARISON OF SWISS LAW AND DELAWARE LAW	11
DESCRIPTION OF DEBT SECURITIES	18
DESCRIPTION OF WARRANTS	24
DESCRIPTION OF UNITS	25
DESCRIPTION OF SUBSCRIPTION RIGHTS	28
PLAN OF DISTRIBUTION	29
LEGAL MATTERS	31
EXPERTS	31
WHERE YOU CAN FIND MORE INFORMATION	31
INCORPORATION OF CERTAIN INFORMATION BY REFERENCE	31

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total aggregate offering price of $300,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The applicable prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading "Where You Can Find More Information" beginning on page 31 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, the accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context indicates otherwise, as used in this prospectus, the terms "CRISPR," "CRISPR Therapeutics," "the Company," "we," "us" and "our" refer to CRISPR Therapeutics AG, a Swiss stock corporation *(Aktiengesellschaft)* and its consolidated subsidiaries. All trademarks or trade names referred to in this prospectus are the property of their respective owners.

Table of Contents

CRISPR THERAPEUTICS AG

Company Overview

We are a leading gene editing company focused on the development of CRISPR/Cas9-based therapeutics. CRISPR/Cas9 stands for Clustered, Regularly Interspaced Short Palindromic Repeats (CRISPR) Associated protein-9 and is a revolutionary technology for gene editing, the process of precisely altering specific sequences of genomic DNA. We are applying this technology to potentially treat a broad set of both rare and common diseases by disrupting, correcting or regulating disease-related genes. We believe that our scientific expertise, together with our gene editing approach, may enable an entirely new class of highly effective and potentially curative treatments for patients for whom current biopharmaceutical approaches have had limited success. Our most advanced programs target beta-thalassemia and sickle cell disease, two hemoglobinopathies that have high unmet medical need.

The use of CRISPR/Cas9 for gene editing was derived from a naturally occurring viral defense mechanism in bacteria and has been described by leading scientific journals as a breakthrough technology. The application of CRISPR/Cas9 for gene editing was co-invented by one of our scientific founders, Dr. Emmanuelle Charpentier, a director of the Max Planck Institute for Infection Biology in Berlin. Dr. Charpentier and her collaborators published work elucidating the mechanism by which the Cas9 endonuclease, a key component of CRISPR/Cas9, can be programmed to cut double-stranded DNA at specific locations. We have acquired rights to the foundational intellectual property encompassing CRISPR/Cas9 and related technologies from Dr. Charpentier, and continue to strengthen our intellectual property estate through our own research and additional in-licensing efforts, furthering our leadership in the development of CRISPR/Cas9-based therapeutics.

Our product development and partnership strategies are designed to exploit the full potential of the CRISPR/Cas9 platform while maximizing the probability of successfully developing our product candidates. We are pursuing a two-pronged product development strategy utilizing both *ex vivo* and *in vivo* approaches. Our most advanced programs use an *ex vivo* approach, whereby cells are harvested from a patient, treated with a CRISPR/Cas9-based therapeutic and reintroduced. We believe that an *ex vivo* approach is less technically challenging than an *in vivo* approach. We have chosen to conduct our lead programs in hemoglobinopathies given the relative ease of editing genes *ex vivo*, the significant unmet medical need associated with beta-thalassemia and sickle cell disease and the well-understood genetics of these diseases. Beyond these lead programs, we are pursuing a number of additional *ex vivo* applications, as well as select *in vivo* applications, whereby the CRISPR/Cas9 product candidate is delivered directly to target cells within the human body. Our initial *in vivo* applications will leverage well-established delivery technologies for gene-based therapeutics.

Given the numerous potential therapeutic applications for CRISPR/Cas9, we have partnered strategically to broaden the indications we can pursue and accelerate development of programs by accessing specific disease-area expertise. In particular, we established a joint venture with Bayer AG and its subsidiaries, or Bayer, in which we have a 50% interest, and a collaboration agreement with Vertex Pharmaceuticals Incorporated, or Vertex, in order to pursue specific indications where these companies have outstanding and distinctive capabilities. The significant resource commitments by our partners underscore the potential of our platform, as well as their dedication to developing transformative CRISPR/Cas9-based treatments.

Our mission is to create transformative gene-based medicines for serious human diseases. We believe that our highly experienced team, together with our scientific expertise, product development strategy, partnerships and intellectual property position us as a leader in the development of CRISPR/Cas9-based therapeutics.

We are a Swiss stock corporation *(Aktiengesellschaft)* organized under the laws of Switzerland. We were incorporated on October 28, 2013 in Basel, Switzerland. Our principal offices are located at Baarerstrasse 14, 6300 Zug, Switzerland and our principal research operations are in Cambridge, Massachusetts. Our telephone number is +41 561 3277 Our website is located at http://www.crisprtx.com. We do not incorporate by reference into this prospectus the information on, or accessible through, our website, and you should not consider it as part of this prospectus.

Table of Contents

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference contain forward-looking statements. These are based on our management's current beliefs, expectations and assumptions about future events, conditions and results and on information currently available to us. Discussions containing these forward-looking statements may be found, among other places, in the Sections entitled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" incorporated by reference from our most recent Annual Report on Form 10-K and other filings we make with the SEC from time to time, which are incorporated by reference herein in their entirety, together with other information in this prospectus, the information and documents incorporated by reference in this prospectus, and in any prospectus supplement or free writing prospectus that we authorize for use in connection with this offering.

Any statements in this prospectus, or incorporated herein, about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements. Within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, these forward-looking statements include statements regarding, among other things, our future discovery and development efforts, our future operating results and financial position, our business strategy, and other objectives for our operations.

In some cases, you can identify forward-looking statements by the words "may," "might," "can," "will," "to be," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "project," "potential," "likely," "continue" and "ongoing," or the negative of these terms, or other comparable terminology intended to identify statements about the future, although not all forward-looking statements contain these words. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements.

You should refer to the "Risk Factors" section contained in the applicable prospectus supplement and under similar headings in the other documents that are incorporated by reference into this prospectus, for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Given these risks, uncertainties and other factors, many of which are beyond our control, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate, and you should not place undue reliance on these forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to revise any forward-looking statements to reflect events or developments occurring after the date of this prospectus, even if new information becomes available in the future.

Table of Contents

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth our ratio of earnings to fixed charges for the periods shown. You should read this table in conjunction with the financial statements and notes incorporated by reference in this prospectus.

	Nine Months Ended September 30, 2017	Years Ended December 31,			Period from October 28, 2013 (inception) to December 31, 2013
		2016	2015	2014	
Ratio of Earnings to Fixed Charges	N/A	N/A	N/A	N/A	N/A

For purposes of calculating the ratios in the table above, earnings consist of net loss before income taxes. Fixed charges include any interest expense on indebtedness and an estimate of the interest expense within rental expense.

Due to our net losses for periods, earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods. The dollar amount of the deficiency in earnings available for fixed charges for periods was approximately $68.4 million, $23.2 million, $25.8 million, $6.8 million and $2.1 million, respectively.

Table of Contents

USE OF PROCEEDS

Except as described in any applicable prospectus supplement, we currently intend to use the net proceeds from the sale of the securities offered under this prospectus for general corporate purposes. General corporate purposes may include research and development and clinical development costs to support the advancement of our product candidates and the expansion of our research development programs; working capital; capital expenditures; office expansion; and other general corporate purposes. We will set forth in the applicable prospectus supplement our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement. Pending these uses, we intend to invest the net proceeds in investment-grade, interest-bearing securities.

Table of Contents

The following summary description of our capital shares is based on the provisions of our articles of association, as well as our organizational rules and the applicable provisions of Swiss law. This information is qualified entirely by reference to the applicable provisions of our articles of association, our organizational rules and Swiss law. For information on how to obtain copies of our articles of association and organizational rules, which are exhibits to our registration statement on Form S-1 filed with the Securities and Exchange Commission, see "Where You Can Find Additional Information."

Share Capital

Our issued share capital is CHF 1,207,610.22 and is fully paid-in. It is divided into 40,253,674 common shares with a nominal value of CHF 0.03 each.

Authorized Share Capital

As of the date of this prospectus, our articles of association authorize the board of directors to increase our share capital at any time until June 30, 2018 by a maximum aggregate amount of CHF 353,970.15 through the issuance of not more than 11,799,005 common shares, which would have to be fully paid-in, with a nominal value of 0.03 CHF each. As of November 1, 2017, we had 41,002,771 common shares outstanding.

Ordinary Capital Increase, Authorized And Conditional Share Capital

Under Swiss law, we may increase our share capital *(Aktienkapital)* with a resolution of the general meeting of shareholders (ordinary capital increase) that must be carried out by the board of directors within three months of the general meeting in order to become effective. Under our articles of association, in the case of subscription and increase against payment of contributions in cash, a resolution passed by a simple majority of the shares represented at the general meeting of shareholders regardless of abstentions or empty or invalid votes is required. In the case of subscription and increase against contributions in kind or to fund acquisitions in kind, when shareholders' statutory pre-emptive rights are withdrawn or where transformation of reserves into share capital is involved, a resolution passed by two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal amount of the shares represented is required.

Furthermore, under the Swiss Code of Obligations, or the CO, our shareholders, by a resolution passed by two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal amount of the shares represented, may empower our board of directors to issue shares of a specific aggregate nominal amount up to a maximum of 50% of the share capital in the form of:

- conditional capital *(bedingtes Kapital)* for the purpose of issuing shares in connection with, among other things, (i) option and conversion rights granted in connection with convertible bonds of the Company or one of our subsidiaries or (ii) grants of rights to employees, members of our board of directors or consultants of the Company or of one of our subsidiaries or other persons providing services to the Company or a subsidiary to subscribe for new shares (conversion or option rights); or

- authorized capital *(genehmigtes Kapital)* to be utilized by the board of directors within a period determined by the shareholders but not exceeding two years from the date of the shareholder approval.

Pre-Emptive Rights

Pursuant to the CO, shareholders have pre-emptive rights *(Bezugsrechte)* to subscribe for new issuances of shares. With respect to conditional capital in connection with the issuance of conversion rights, convertible bonds or similar debt instruments, shareholders have advance subscription rights *(Vorwegzeichnungsrechte)* for the subscription of conversion rights, convertible bonds or similar debt instruments.

A resolution passed at a general meeting of shareholders by two-thirds of the shares represented and the absolute majority of the nominal value of the shares represented may authorize our board of directors to withdraw or limit pre-emptive rights or advance subscription rights in certain circumstances.

If pre-emptive rights are granted, but not exercised, the board of directors may allocate the pre-emptive rights as it elects.

Table of Contents

With respect to our authorized share capital, the board of directors is authorized by our articles of association to withdraw or to limit the pre-emptive rights of shareholders, and to allocate them to third parties or to us, in the event that the newly issued shares are used for the following purposes:

- if the issue price of the new registered shares is determined by reference to the market price;
- for the acquisition of an enterprise, part(s) of an enterprise or participations, or for the financing or refinancing of any of such transactions, or in the event of share placement for the financing or refinancing of such transactions;
- for purposes of broadening the shareholder constituency of the Company in certain financial or investor markets, for purposes of the participation of strategic partners, or in connection with the listing or registration of new registered shares on domestic or foreign stock exchanges;
- for purposes of granting an over-allotment option of up to 20% of the total number of registered shares in a placement or sale of registered shares to the respective initial purchaser(s) or underwriter(s);
- for raising of capital (including private placements) in a fast and flexible manner which probably could not be reached without the exclusion of the statutory pre-emptive right of the existing shareholders;
- following a shareholder or a group of shareholders acting in concert having accumulated shareholdings in excess of 15% of the share capital registered in the commercial register without having submitted to the other shareholders a takeover offer recommended by the board of directors, or for the defense of an actual, threatened or potential takeover bid, in relation to which the board of directors, upon consultation with an independent financial adviser retained by it, has not recommended to the shareholders acceptance on the basis that the board of directors has not found the takeover bid to be financially fair to the shareholders; or
- for other valid grounds in the sense of Article 652b para. 2 of the CO.

Conditional Share Capital for Bonds and Similar Debt Instruments

Our share capital may be increased by a maximum aggregate amount of CHF 147,591.00 through the issuance of not more than 4,919,700 common shares, which would have to be fully paid-in, with a nominal value of CHF 0.03 each, by the exercise of conversion and/or option or warrant rights granted in connection with bonds or similar instruments of the Company or one of our subsidiaries, including convertible debt instruments. Shareholders will not have pre-emptive rights in such circumstances. The holders of convertible bonds are entitled to the new shares upon the occurrence of the applicable conversion feature.

When issuing convertible bonds, the board of directors is authorized to withdraw or to limit the advance right of shareholders to subscribe to the convertible bond issuance:

- for the purpose of financing or refinancing the acquisition of enterprises, divisions thereof, or of participations or of newly planned investments of the Company; or
- if the issuance occurs in international capital markets or through private placements.

To the extent that the advance subscription rights are withdrawn, (i) the instruments are to be issued at market conditions; (ii) the term to exercise the option or conversion rights may not exceed 10 years as of the date of the issuance for warrants and twenty years for conversion rights; and (iii) the exercise price for the new shares must at least correspond to the market conditions at the time of the issuance of the instruments.

Conditional Share Capital for Employee Benefit Plans

Our share capital may, to the exclusion of the pre-emptive rights of shareholders, be increased by a maximum aggregate amount of CHF 372,557.73 through the issuance of not more than 12,418,591 common shares, which would have to be fully paid-in, with a nominal value of CHF 0.03 each, by the exercise of option or conversion rights that have been granted to employees, members of the board of directors or consultants of the Company or of one of our subsidiaries or other persons providing services to the Company or a subsidiary through one or more employee benefit plans created by the board of directors.

Table of Contents

Uncertificated Securities

Our shares are uncertificated securities *(Wertrechte,* within the meaning of art. 973c of the CO) and, when administered by a financial intermediary *(Verwahrungsstelle,* within the meaning of the Federal Act on Intermediated Securities, "FISA"), qualify as intermediated securities *(Bucheffekten,* within the meaning of the FISA). In accordance with art. 973c of the CO, we maintain a non-public register of uncertificated securities *(Wertrechtebuch).* We may at any time convert uncertificated securities into share certificates (including global certificates), one kind of certificate into another, or share certificates (including global certificates) into uncertificated securities. Following entry in the share register, a shareholder may at any time request from us a written confirmation in respect of the shares held by such shareholder, as reflected in the share register. Shareholders are not entitled, however, to request the printing and delivery of certificates. We may print and deliver certificates for shares at any time.

Voting Rights

The shareholders exercise their voting rights at the general meetings of shareholders in proportion to the nominal value of the shares belonging to them. The holders of our common shares do not have cumulative voting rights in the election of directors, as cumulative voting is not permitted under Swiss law. The shares are not divisible. The right to vote and the other rights of share ownership may only be exercised by shareholders (including any nominees) or usufructuaries who are entered in our share register at the cut-off date determined by the board of directors and by persons who are entitled by law to the voting right of a share. Each shareholder may be represented by the independent proxy holder (annually elected by the general meeting of shareholders), another registered shareholder or third person with written authorization to act as proxy or the shareholder's legal representative. The requirements regarding powers of attorney and instructions are determined by the board of directors.

Our articles contain provisions that prevent investors from acquiring voting rights exceeding 15% of the outstanding share capital. Specifically, no individual or legal entity may, directly or indirectly, control voting rights with respect to 15% or more of the registered share capital recorded in the Commercial Register. In the event that a shareholder should exceed the 15% ownership threshold, the registered shares exceeding the limit of 15% shall be entered in our share registered as shares without voting rights. The board of directors may in special cases approve exceptions to the above regulations.

Furthermore, with respect to our authorized share capital, the board of directors is authorized to withdraw or limit the preemptive rights of the shareholders and to allot them to third parties following a shareholder or a group of shareholders acting in concert having accumulated shareholdings in excess of 15% of the share capital registered in the commercial register without having submitted to the other shareholders a takeover offer recommended by the board of directors, or for the defense of an actual, threatened or potential takeover bid, in relation to which the board of directors, upon consultation with an independent financial adviser retained by it, has not recommended to the shareholders acceptance on the basis that the board of directors has not found the takeover bid to be financially fair to the shareholders.

Our articles contain provisions that persons who do not expressly declare in the registration application that they are holding the shares on their own account (thereafter: nominees) shall forthwith be entered on the share register as shareholders with voting rights up to a maximum of 3% of the share capital. Beyond that limit, registered shares of nominees shall only be entered as voting if the nominees in question confirm in writing that they are willing to disclose the names, addresses and shareholdings of the persons on whose account they hold 0.5% or more of the share capital. The board of directors concludes agreements with nominees that among other things govern the representation of shareholders and the voting rights.

Registration Rights

We and some of the holders of our common shares have entered into a registration rights agreement. The registration rights provisions of this agreement provide those holders with demand, piggyback and Form S-3 registration rights with respect to the common shares currently held by them.

Demand Registration Rights

The holders of the registrable securities are entitled to certain demand registration rights. The holders of at least two-thirds (66 2/3%) of the registrable securities then outstanding may make a written request that we register all or a portion of their registrable securities, subject to certain specified exceptions. Such request for registration must cover securities the aggregate

proceeds of which, after payment of underwriting discounts, commissions and other expenses related to such registration, would exceed $10,000,000. In no event will we be required to effect more than two (2) demand registrations.

Piggyback Registration Rights

If we propose to register for offer and sale any of our securities under the Securities Act in another offering for cash, either for our own account or for the account of other security holders, the holders of registrable securities will be entitled to certain "piggyback" registration rights allowing them to include their registrable securities in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act in connection with a public offering for our own account or for the account of any shareholder, the holders of these registrable securities are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their registrable securities in the registration.

Table of Contents

Registration on Form S-3

The holders of registrable securities are entitled to certain Form S-3 registration rights. Any holder of registrable securities can make a request that we register for offer and sale all or any portion of their registrable securities on Form S-3 or any similar short form registration statement if we are qualified to file a registration statement on Form S-3, subject to certain specified exceptions. Such request for registration on Form S-3 must cover securities the aggregate offering price of which, before payment of the underwriting discounts and commissions, equals or exceeds $2.0 million. We will not be required to effect more than one (1) registration on Form S-3 within any 12-month period.

Expenses of Registration

We will pay all expenses relating to any demand, piggyback or Form S-3 registration, other than underwriting discounts and commissions, subject to specified conditions and limitations.

Termination of Registration Rights

The registration rights granted under the registration rights agreement will terminate upon the fifth anniversary of the completion of our initial public offering, which would be in October 2021, or, if earlier, with respect to a particular holder, at such time as that holder and its affiliates may sell all of their common shares pursuant to Rule 144 under the Securities Act of 1933, as amended, without any restrictions on volume.

Table of Contents

COMPARISON OF SWISS LAW AND DELAWARE LAW

The Swiss laws applicable to Swiss corporations and their shareholders differ from laws applicable to U.S. corporations and their shareholders. The following table summarizes significant differences in shareholder rights between the provisions of the Swiss Code of Obligations *(Schweizerisches Obligationenrecht)* and the Swiss Ordinance against excessive compensation in listed stock corporations applicable to our Company, as implemented by the Company in its Articles of Association, and the Delaware General Corporation Law applicable to companies incorporated in Delaware and their shareholders. Please note that this is only a general summary of certain provisions applicable to companies in Delaware. Certain Delaware companies may be permitted to exclude certain of the provisions summarized below in their charter documents.

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
Mergers and similar arrangements	
Under the Delaware General Corporation Law, with certain exceptions, a merger, consolidation, sale, lease or transfer of all or substantially all of the assets of a corporation must be approved by the board of directors and a majority of the outstanding shares entitled to vote thereon. A shareholder of a Delaware corporation participating in certain major corporate transactions may, under certain circumstances, be entitled to appraisal rights pursuant to which such shareholder may receive cash in the amount of the fair value of the shares held by such shareholder (as determined by a court) in lieu of the consideration such shareholder would otherwise receive in the transaction. The Delaware General Corporation Law also provides that a parent corporation, by resolution of its board of directors, may merge with any subsidiary, of which it owns at least 90.0% of each class of share capital without a vote by the shareholders of such subsidiary. Upon any such merger, dissenting shareholders of the subsidiary would have appraisal rights.	Under Swiss law, with certain exceptions, a merger or a demerger of the corporation or a sale of all or substantially all of the assets of a corporation must be approved by two-thirds of the voting rights represented at the respective general meeting of shareholders as well as the absolute majority of the nominal value of shares represented at such shareholders' meeting. A shareholder of a Swiss corporation participating in a statutory merger or demerger pursuant to the Swiss Merger Act *(Fusionsgesetz)* can file a lawsuit against the surviving company. If the consideration is deemed "inadequate," such shareholder may, in addition to the consideration (be it in shares or in cash) receive an additional amount to ensure that such shareholder receives the fair value of the shares held by such shareholder. Swiss law also provides that if the merger agreement provides only for a compensation payment, at least 90.0% of all members in the transferring legal entity, who are entitled to vote, shall approve the merger agreement.
Shareholders' suits	
Class actions and derivative actions generally are available to shareholders of a Delaware corporation for, among other things, breach of fiduciary duty, corporate waste and actions not taken in accordance with applicable law. In such actions, the court has discretion to permit the winning party to recover attorneys' fees incurred in connection with such action.	Class actions and derivative actions as such are not available under Swiss law. Nevertheless, certain actions may have a similar effect. A shareholder is entitled to bring suit against directors for breach of their duties and claim the payment of the company's losses or damages both to the corporation and, subject to certain conditions, to the individual shareholder and creditors. Likewise, an appraisal lawsuit won by a shareholder may indirectly compensate all shareholders. Under Swiss law, the winning party is generally entitled to recover or to partially recover attorneys' fees incurred in connection with such action, *provided, however,* that the court has broad discretion to permit the shareholder whose claim has been dismissed to recover attorneys' fees incurred to the extent he or she acted in good faith.

Table of Contents

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
Shareholder vote on board and management compensation	
Under the Delaware General Corporation Law, the board of directors has the authority to fix the compensation of directors, unless otherwise restricted by the certificate of incorporation or bylaws.	Pursuant to the Swiss Ordinance against excessive compensation in listed stock corporations *(Verordnung gegen übermässige Vergütungen bei börsenkotierten Aktiengesellschaften),* the general meeting of shareholders has the non-transferable right, amongst others, to vote on the fixed and on the variable compensation of the members of the board of directors, of the executive management and of the advisory boards.
Annual vote on board renewal	
Unless directors are elected by written consent in lieu of an annual meeting, directors are elected in an annual meeting of stockholders on a date and at a time designated by or in the manner provided in the bylaws. Re-election is possible. Classified boards are permitted.	The general meeting of shareholders elects annually (i.e. term of office until the end of the following general meeting of shareholders) the members of the board of directors and the members of the compensation, committee individually for a term of office of one year. Re-election is possible.
Indemnification of directors and executive management and limitation of liability	
The Delaware General Corporation Law provides that a certificate of incorporation may contain a provision eliminating or limiting the personal liability of directors (but not other controlling persons) of the corporation for monetary damages for breach of a fiduciary duty as a director, except no provision in the certificate of incorporation may eliminate or limit the liability of a director for: • any breach of a director's duty of loyalty to the corporation or its shareholders; • acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law; • statutory liability for unlawful payment of dividends or unlawful stock purchase or redemption; or • any transaction from which the director derived an improper personal benefit.	Under Swiss corporate law, an indemnification by the corporation of a director or member of the executive management in relation to potential personal liability is not effective to the extent the director or member of the executive management intentionally or negligently violated his or her corporate duties towards the corporation. (Certain views advocate that at least a grossly negligent violation is required to exclude the indemnification.) Furthermore, the general meeting of shareholders may discharge the directors and members of the executive management from liability from actions taken during the past financial year. Such discharge is effective only, however, for disclosed facts and only as against the company and those shareholders who approved the discharge or who have since acquired their shares in full knowledge of the discharge. Most violations of corporate law are regarded as violations of duties towards the corporation rather than towards the shareholders. In addition, indemnification of other controlling persons is not permitted under Swiss corporate law, including shareholders of the corporation.
A Delaware corporation may indemnify any person who was or is a party or is threatened to be made a party to any proceeding, other than an action by or on behalf of the corporation, because the person is or was a director or officer, against liability incurred in connection with the proceeding if the director or officer acted in good faith and in a manner reasonably believed to be in, or not opposed to, the best interests of the corporation; and the director or officer, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful.	The articles of association of a Swiss corporation may also set forth that the corporation shall indemnify and hold harmless, to the extent permitted by the law, the directors and executive managers out of assets of the corporation against threatened, pending or completed actions. Also, a corporation may enter into and pay for directors' and officers' liability insurance which may cover negligent acts as well.

Table of Contents

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
Unless ordered by a court, any foregoing indemnification is subject to a determination that the director or officer has met the applicable standard of conduct: • by a majority vote of the directors who are not parties to the proceeding, even though less than a quorum; • by a committee of directors designated by a majority vote of the eligible directors, even though less than a quorum; • by independent legal counsel in a written opinion if there are no eligible directors, or if the eligible directors so direct; or • by the shareholders. Moreover, a Delaware corporation may not indemnify a director or officer in connection with any proceeding in which the director or officer has been adjudged to be liable to the corporation unless and only to the extent that the court determines that, despite the adjudication of liability but in view of all the circumstances of the case, the director or officer is fairly and reasonably entitled to indemnity for those expenses which the court deems proper.	
Directors' fiduciary duties	
A director of a Delaware corporation has a fiduciary duty to the corporation and its shareholders. This duty has two components: • the duty of care; and • the duty of loyalty. The duty of care requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself or herself of, and disclose to shareholders, all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he or she reasonably believes to be in the best interests of the corporation. He or she must not use his or her corporate position for personal gain or advantage. This duty prohibits self-dealing by a director and mandates that the best interest of the corporation and its shareholders take precedence over any interest possessed by a director, officer or controlling shareholder and not shared by the shareholders generally. In general, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties.	The board of directors of a Swiss corporation manages the business of the corporation, unless responsibility for such management has been delegated to the executive management (for example by organizational rules and comparable bylaws). However, there are several non-transferable duties of the board of directors: • the overall management of the corporation and the issuing of all necessary directives; • the determination of the corporation's organization; • the organization of the accounting, financial control and financial planning systems as required for the management of the corporation; • the appointment and dismissal of persons entrusted with managing and representing the corporation; • overall supervision of the persons entrusted with managing the corporation, in particular with regard to compliance with the law, articles of association, operational regulations and directives; • compilation of the annual report, preparation for the general meeting, the compensation report and implementation of its resolutions; and • notification of the court in the event that the company is over-indebted.

Table of Contents

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
Should such evidence be presented concerning a transaction by a director, a director must prove the procedural fairness of the transaction, and that the transaction was of fair value to the corporation.	The members of the board of directors must perform their duties with all due diligence and safeguard the interests of the corporation in good faith. They must afford the shareholders equal treatment in equal circumstances. The burden of proof for a violation of these duties is with the corporation or with the shareholder bringing a suit against the director.
Shareholder action by written consent	
A Delaware corporation may, in its certificate of incorporation, eliminate the right of shareholders to act by written consent.	Shareholders of a Swiss corporation may only exercise their voting rights in a general meeting of shareholders and may not act by written consents. The articles of association must allow for (independent) proxies to be present at a general meeting of shareholders. The instruction of such (independent) proxies may occur in writing or electronically.
Shareholder proposals	
A shareholder of a Delaware corporation has the right to put any proposal before the annual meeting of shareholders, provided it complies with the notice provisions in the governing documents. A special meeting may be called by the board of directors or any other person authorized to do so in the governing documents, but shareholders may be precluded from calling special meetings.	At any general meeting of shareholders any shareholder may put proposals to the meeting if the proposal is part of an agenda item. No resolution may be made on proposals relating to the agenda items that were not duly notified. Unless the articles of association provide for a lower threshold or for additional shareholders' rights: • shareholders together representing at least 10% of the share capital may demand that a general meeting of shareholders be called for specific agenda items and specific proposals; and • shareholders together representing shares with a nominal value of at least CHF 1.0 million may demand that an agenda item including a specific proposal be put on the agenda for a regularly scheduled general meeting of shareholders, provided such request is made with appropriate notice. Any shareholder can propose candidates for election as directors provided that the election of board members and the names of the candidates have been included as an agenda item. In addition, any shareholder is entitled, at a general meeting of shareholders and without advance notice, to (i) request information from the board on the affairs of the company (note, however, that the right to obtain such information is limited), (ii) request information from the auditors on the methods and results of their audit, (iii) request to convene an extraordinary general meeting or (iv) request to carry out a special audit and to appoint a special auditor.

Table of Contents

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
Cumulative voting	
Under the Delaware General Corporation Law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation provides for it.	Cumulative voting is not permitted under Swiss corporate law. Pursuant to Swiss law, shareholders can vote for each proposed candidate, but they are not allowed to cumulate their votes for single candidates. An annual individual election of (i) all members of the board of directors, (ii) the chairman of the board of directors, (iii) the members of the compensation committee, (iv) the election of the independent proxy for a term of office of one year (i.e. until the following annual general meeting) as well as the vote on the compensation for the members of the board of directors and the executive management as well as for the members of the advisory board, if applicable, is mandatory for listed companies. Re-election is permitted.
Removal of directors	
A Delaware corporation with a classified board may be removed only for cause with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise.	A Swiss corporation may remove, with or without cause, any director at any time with a resolution passed by a simple majority of the shares represented at a general meeting of shareholders. The articles of association may require the approval by a qualified majority of the shares represented at a meeting for the removal of a director.
Transactions with interested shareholders	
The Delaware General Corporation Law generally prohibits a Delaware corporation from engaging in certain business combinations with an "interested shareholder" for three years following the date that such person becomes an interested shareholder. An interested shareholder generally is a person or group who or which owns or owned 15.0% or more of the corporation's outstanding voting stock within the past three years.	No such rule applies to a Swiss corporation.
Dissolution; Winding up	
Unless the board of directors of a Delaware corporation approves the proposal to dissolve, dissolution must be approved by shareholders holding 100.0% of the total voting power of the corporation. Only if the dissolution is initiated by the board of directors may it be approved by a simple majority of the corporation's outstanding shares. Delaware law allows a Delaware corporation to include in its certificate of incorporation a supermajority voting requirement in connection with dissolutions initiated by the board.	A dissolution of a Swiss corporation requires the approval by two-thirds of the voting rights represented as well as the absolute majority of the nominal value of the share capital represented at a general meeting of shareholders passing a resolution on such dissolution. The articles of association may increase the voting thresholds required for such a resolution.

Table of Contents

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
Variation of rights of shares	
A Delaware corporation may vary the rights of a class of shares with the approval of a majority of the outstanding shares of such class, unless the certificate of incorporation provides otherwise.	The general shareholder meeting of a Swiss corporation may resolve that preference shares be issued or that existing shares be converted into preference shares with a resolution passed by a simple majority of the shares represented at the general meeting of shareholders. Where a company has issued preference shares, further preference shares conferring preferential rights over the existing preference shares may be issued only with the consent of both a special meeting of the adversely affected holders of the existing preference shares and of a general meeting of all shareholders, unless otherwise provided in the articles of association. Shares with preferential voting rights are not regarded a special class for these purposes.
Amendment of governing documents	
A Delaware corporation's governing documents may be amended with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise.	The articles of association of a Swiss corporation may be amended with a resolution passed by a simple majority of the shares represented at such meeting, unless otherwise provided in the articles of association. There are a number of resolutions, such as an amendment of the stated purpose of the corporation, the introduction of authorized and conditional capital and the introduction of shares with preferential voting rights that require the approval by two-thirds of the voting rights represented and an absolute majority of the nominal value of the shares represented at a shareholders' meeting. The articles of association may increase the voting thresholds.
Inspection of books and records	
Shareholders of a Delaware corporation, upon written demand under oath stating the purpose thereof, have the right during the usual hours for business to inspect for any proper purpose, and to obtain copies of list(s) of shareholders and other books and records of the corporation and its subsidiaries, if any, to the extent the books and records of such subsidiaries are available to the corporation.	Shareholders of a Swiss corporation may only inspect books and records if the general meeting of shareholders or the board of directors approved such inspection. The information may be refused where providing it would jeopardize the corporation's trade secrets or other interests warranting protection. A shareholder is only entitled to receive information to the extent required to exercise such shareholders' rights, subject to the interests of the corporation. The right to inspect the share register is limited to the right to inspect that shareholder's own entry in the share register.
Payment of dividends	

The board of directors may approve a dividend without shareholder approval. Subject to any restrictions contained in its certificate of incorporation, the board may declare and pay dividends upon the shares of its share capital either:

- out of its surplus; or
- in case there is no such surplus, out of its net profits for the fiscal year in which the dividend is declared and/or the preceding fiscal year.

Stockholder approval is required to authorize share capital in excess of that provided in the charter. Directors may issue authorized shares without stockholder approval.

Dividend payments are subject to the approval of the general meeting of shareholders. The board of directors may propose to shareholders that a dividend shall be paid but cannot itself authorize the distribution.

Payments out of the Company's share capital (in other words, the aggregate nominal value of the Company's registered share capital) in the form of dividends are not allowed; however, payments out of share capital may be made by way of a capital reduction only. Dividends may be paid only from the profits brought forward from the previous business years or if the Company has distributable reserves, each as will be presented on the Company's audited annual stand-alone balance sheet. The dividend may be determined only after the allocations to reserves required by the law and the articles of association have been deducted.

Table of Contents

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
Creation and issuance of new shares	
All creation of shares require the board of directors to adopt a resolution or resolutions, pursuant to authority expressly vested in the board of directors by the provisions of the company's certificate of incorporation.	All creation of shares requires a shareholders' resolution. An authorized or contingent capital increase requires at least two-thirds of the voting rights represented at the general meeting of shareholders and an absolute majority of the nominal value of shares represented. Authorized shares can be, once created by shareholder resolution, issued by the board of directors (subject to fulfillment of the authorization). Conditional shares are created and issued through the exercise of options and conversion rights related to debt instruments issued by the board of directors or such rights issued to employees.

Transfer Agent And Registrar

The transfer agent and registrar for our common shares is American Stock Transfer & Trust Company, and its address is 6201 5th Street, Brooklyn, NY 11219.

Listing on the NASDAQ Global Market

Our common shares are listed on the NASDAQ Global Market under the symbol "CRSP."

Table of Contents

DESCRIPTION OF DEBT SECURITIES

This section describes the general terms and provisions of our debt securities that we may issue from time to time. We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, the applicable prospectus supplement will describe the specific terms of any debt securities offered through that prospectus supplement. The terms of any debt securities we offer under a prospectus supplement may differ from the terms we describe below. Unless the context requires otherwise, whenever we refer to the "indentures," we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue any senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue any subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement, of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The indentures will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We use the term "trustee" to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplement and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete applicable indenture that contains the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title;
- the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;
- any limit on the amount that may be issued;
- whether or not we will issue the series of debt securities in global form, and, if so, the terms and who the depository will be;
- the maturity date;
- whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;
- the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- the terms of the subordination of any series of subordinated debt;
- the place where payments will be payable;
- restrictions on transfer, sale or other assignment, if any;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;

- the date, if any, after which, the conditions upon which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;

Table of Contents

- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option, to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- whether the indenture will restrict our ability or the ability of our subsidiaries to:
  - incur additional indebtedness;
  - issue additional securities;
  - create liens;
  - pay dividends or make distributions in respect of our share capital or the share capital of our subsidiaries;
  - redeem share capital;
  - place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;
  - make investments or other restricted payments;
  - sell or otherwise dispose of assets;
  - enter into sale-leaseback transactions;
  - engage in transactions with shareholders or affiliates;
  - issue or sell shares of our subsidiaries; or
  - effect a consolidation or merger;
- whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;
- a discussion of certain material or special United States federal income tax considerations applicable to the debt securities;
- information describing any book-entry features;
- provisions for a sinking fund purchase or other analogous fund, if any;
- the applicability of the provisions in the indenture on discharge;
- whether the debt securities are to be offered at a price such that they will be deemed to be offered at an "original issue discount" as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;
- the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations or advisable in connection with the marketing of the debt securities.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common shares or other securities (including securities of a third-party). We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of our common shares or other securities (including securities of a third-party) that the holders of the series of debt securities receive would be subject to adjustment.

Table of Contents

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for other securities of ours or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default Under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended;
- if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable at maturity, upon redemption or repurchase or otherwise, and the time for payment has not been extended;
- if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

We will describe in each applicable prospectus supplement any additional events of default relating to the relevant series of debt securities.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the unpaid principal, premium, if any, and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity or security satisfactory to it against any loss, liability or expense. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the trustee or security satisfactory to it against any loss, liability or expense or to be incurred in compliance with instituting the proceeding as trustee; and

Table of Contents

- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities, or other defaults that may be specified in the applicable prospectus supplement.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indentures.

Modification of Indenture; Waiver

Subject to the terms of the indenture for any series of debt securities that we may issue, we and the trustee may change an indenture without the consent of any holders with respect to the following specific matters:

- to fix any ambiguity, defect or inconsistency in the indenture;
- to comply with the provisions described above under "Description of Our Debt Securities—Consolidation, Merger or Sale;"
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under "Description of Debt Securities—General," to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment hereunder by a successor trustee;
- to provide for uncertificated debt securities and to make all appropriate changes for such purpose;
- to add to our covenants such new covenants, restrictions, conditions or provisions for the benefit of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred to us in the indenture; or
- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, subject to the terms of the indenture for any series of debt securities that we may issue or as otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the stated maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that, subject to the terms of the indenture and any limitation otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- register the transfer or exchange of debt securities of the series;

Table of Contents

- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series. If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Table of Contents

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Ranking of Debt Securities

The subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

The senior debt securities will rank equally in right of payment to all our other senior unsecured debt. The senior indenture does not limit the amount of senior debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

Table of Contents

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement, which includes this prospectus.

General

We may issue warrants for the purchase of common shares and/or debt securities in one or more series. We may issue warrants independently or together with common shares and/or debt securities, and the warrants may be attached to or separate from these securities.

We will evidence each series of warrants by warrant certificates that we will issue under a separate warrant agreement. We will enter into the warrant agreement with a warrant agent. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common shares, the number of common shares purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the periods during which, and places at which, the warrants are exercisable;
- the manner of exercise;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreement and warrants may be modified;
- federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Table of Contents

DESCRIPTION OF UNITS

We may issue units comprised of common shares, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue 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 of the governing unit agreement;
- the price or prices at which such units will be issued;
- the applicable United States federal income tax considerations relating to the units;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Share Capital,” “Description of Debt Securities” and “Description of Warrants” will apply to the securities included in each unit, to the extent relevant and as may be updated in any prospectus supplements.

Issuance in Series

We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of a particular series of units will be described in the applicable prospectus supplement.

Unit Agreements

We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement:

Modification Without Consent

We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

- to cure any ambiguity; any provisions of the governing unit agreement that differ from those described below;
- to correct or supplement any defective or inconsistent provision; or

- to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

Table of Contents

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification with Consent

We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

- impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or
- reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

- If the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or
- If the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document.

In each case, the required approval must be given by written consent.

Unit Agreements Will Not Be Qualified Under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

Mergers and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Governing Law

The unit agreements and the units will be governed by New York law.

Form, Exchange and Transfer

We will issue each unit in global—i.e., book-entry—form only. Units in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depositary's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. We will describe

book-entry securities, and other terms regarding the issuance and registration of the units in the applicable prospectus supplement.

Table of Contents

Each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them.

The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.

- Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.
- Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with the holder's proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.
- If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning fifteen (15) days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depositary will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

Payments and Notices

In making payments and giving notices with respect to our units, we will follow the procedures as described in the applicable prospectus supplement.

Table of Contents

DESCRIPTION OF OUR SUBSCRIPTION RIGHTS

The following is a general description of the terms of the subscription rights we may issue from time to time. Particular terms of any subscription rights we offer will be described in the prospectus supplement or free writing prospectus relating to such subscription rights, and may differ from the terms described herein.

We may issue subscription rights to purchase our securities. These subscription rights may be issued independently or together with any other security offered hereby and may or may not be transferable by the shareholder receiving the subscription rights in such offering. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering.

The applicable prospectus supplement will describe the specific terms of any offering of subscription rights for which this prospectus is being delivered, including the following:

- whether common shares, preferred shares or warrants for those securities will be offered under the shareholder subscription rights;
- the price, if any, for the subscription rights;
- the exercise price payable for each security upon the exercise of the subscription rights;
- the number of subscription rights issued to each shareholder;
- the number and terms of the securities which may be purchased per each subscription right;
- the extent to which the subscription rights are transferable;
- any other terms of the subscription rights, including the terms, procedures and limitations relating to the exchange and exercise of the subscription rights;
- the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;
- the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities;
- if appropriate, a discussion of material U.S. federal income tax considerations; and
- if applicable, the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering of subscription rights.

The description in the applicable prospectus supplement of any subscription rights we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable subscription rights certificate or subscription rights agreement, which will be filed with the SEC if we offer subscription rights.

Standby Arrangements

If fewer than all of the subscription rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than shareholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. 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; or
- at negotiated prices.

We may also sell equity securities covered by this registration statement in an "at–the-market offering" as defined in Rule 415 under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price on or through the facilities of the NASDAQ Global Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale.

Such at-the-market offerings, if any, may be conducted by underwriters acting as principal or agent.

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

- the name or names of any underwriters, dealers or agents, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts or concessions allowed or re-allowed or paid to dealers;
- the terms of any subscription rights; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are 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. Any public offering price and any discounts 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 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.

Table of Contents

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

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids. 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. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any 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 Rule 103 of 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.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

Direct sales to investors or our shareholders may be accomplished through subscription offerings or through subscription rights distributed to shareholders. In connection with subscription offerings or the distribution of subscription rights to shareholders, if all of the underlying securities are not subscribed for, we may sell any unsubscribed securities to third parties directly or through underwriters or agents. In addition, whether or not all of the underlying securities are subscribed for, we may concurrently offer additional securities to third parties directly or through underwriters or agents. If securities are to be sold through subscription rights, the subscription rights will be distributed as a dividend to the shareholders for which they will pay no separate consideration.

Table of Contents

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, certain legal matters in connection with the offering and the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon by Goodwin Procter LLP, Boston, Massachusetts.

EXPERTS

The financial statements of CRISPR Therapeutics AG appearing in CRISPR Therapeutics AG's Annual Report (Form 10-K) for the year ended December 31, 2016, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You should rely only on the information contained in this prospectus or incorporated by reference. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement, as well as any other document filed by us with the SEC, at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. You can also request copies of these documents by writing to the SEC and paying a fee for the copying cost. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including CRISPR Therapeutics AG. The address of the SEC website is www.sec.gov.

We maintain a website at www.crisprtx.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The SEC file number for the documents incorporated by reference in this prospectus is 001-37923. The documents incorporated by reference into this prospectus contain important information that you should read about us.

The following documents are incorporated by reference into this document:

- our Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on March 10, 2017;
- our Quarterly Report on Form 10-Q for the three months ended March 31, 2017 filed with the SEC on May 11, 2017;
- our Quarterly Report on Form 10-Q for the three months ended June 30, 2017 filed with the SEC on August 10, 2017;
- our Quarterly Report on Form 10-Q for the three months ended September 30, 2017 filed with the SEC on November 8, 2017;

- our Current Reports on Form 8-K filed with the SEC on November 7, 2017, October 2, 2017, July 27, 2017, July 25, 2017, June 19, 2017, June 8, 2017, June 2, 2017, May 4, 2017, April 27, 2017, April 13, 2017, March 31, 2017, March 20, 2017 and February 15, 2017, to the extent the information in such reports is filed and not furnished;

Table of Contents

- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2016 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 18, 2017; and
- the description of our common shares contained in our Registration Statement on Form 8-A12B, filed with the SEC on October 18, 2016, including any amendments or reports filed for the purposes of updating this description.

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus forms a part and prior to effectiveness of the registration statement, or (ii) after the date of this prospectus but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into such documents. You should direct any requests for documents to CRISPR Therapeutics, Inc., 610 Main Street, Cambridge, Massachusetts 02139, Attn: Secretary, telephone: (617) 315-4626.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

Table of Contents

5,000,000

CRISPR Therapeutics AG

Common Shares

PROSPECTUS SUPPLEMENT

Goldman Sachs & Co. LLC **Piper Jaffray** **Barclays**

Guggenheim Securities

January 4, 2018