Intellia Therapeutics, Inc.
Form 10-Q
May 01, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-Q

QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the quarterly period ended March 31, 2018

OR

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

Commission File Number: 001-37766

INTELLIA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

| | |
|---|---|
| Delaware<br>(State or other jurisdiction of<br>incorporation or organization) | 36-4785571<br>(I.R.S. Employer<br>Identification No.) |
| 40 Erie Street, Suite 130, Cambridge, Massachusetts<br>(Address of principal executive offices) | 02139<br>(Zip code) |

857-285-6200

(Registrant’s telephone number, including area code)

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See definitions of “large accelerated filer,” “accelerated filer,” “smaller reporting company,” and “emerging growth company” in Rule 12b-2 of the Exchange Act.

| | | |
|---|---|---|
| Large accelerated filer | | Accelerated filer |
| Non-accelerated filer | (Do not check if a smaller reporting company) | Smaller reporting company |
| Emerging growth company | | |

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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

The number of shares outstanding of the registrant’s common stock as of April 27, 2018: 43,089,810 shares.

PART I - FINANCIAL INFORMATION

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PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

INTELLIA THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS (UNAUDITED)

(Amounts in thousands except share and per share data)

| | March 31, 2018 | December 31, 2017 |
|---|---|---|
| ASSETS | | |
| Current Assets: | | |
| Cash and cash equivalents | $327,778 | $ 340,678 |
| Accounts receivable | 7,466 | 10,471 |
| Prepaid expenses and other current assets | 2,476 | 3,681 |
| Total current assets | 337,720 | 354,830 |
| Property and equipment, net | 16,010 | 15,272 |
| Other assets | 5,815 | 6,133 |
| Total Assets | $359,545 | $ 376,235 |
| LIABILITIES AND STOCKHOLDERS' EQUITY | | |
| Current Liabilities: | | |
| Accounts payable | $1,916 | $ 2,172 |
| Accrued expenses | 6,605 | 7,999 |
| Current portion of deferred revenue | 17,062 | 21,188 |
| Total current liabilities | 25,583 | 31,359 |
| Deferred revenue, net of current portion | 38,332 | 44,111 |
| Other long-term liabilities | 131 | 168 |
| Commitments and contingencies | | |
| Stockholders' Equity: | | |
| Common stock, $0.0001 par value; 120,000,000 shares authorized, 43,091,922 shares and 42,384,623 shares issued and outstanding, respectively | 4 | 4 |
| Additional paid-in capital | 432,533 | 421,706 |
| Accumulated deficit | (137,038) | (121,113) |
| Total stockholders' equity | 295,499 | 300,597 |
| Total Liabilities and Stockholders' Equity | $359,545 | $ 376,235 |

See notes to consolidated financial statements.

INTELLIA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS (UNAUDITED)

(Amounts in thousands except per share data)

| | Three Months Ended March 31, | |
|---|---|---|
| | 2018 | 2017 |
| Collaboration revenue | $7,469 | $6,215 |
| Operating expenses: | | |
| Research and development | 22,493 | 13,431 |
| General and administrative | 7,406 | 5,732 |
| Total operating expenses | 29,899 | 19,163 |
| Operating loss | (22,430) | (12,948) |
| Interest income | 1,074 | 317 |
| Net loss | $(21,356) | $(12,631) |
| Net loss per share attributable to common stockholders, basic and diluted | $(0.51) | $(0.36) |
| Weighted average shares outstanding, basic and diluted | 42,043 | 34,723 |

See notes to consolidated financial statements.

INTELLIA THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS (UNAUDITED)

(Amounts in thousands)

| | Three Months Ended March 31, | |
|---|---|---|
| | 2018 | 2017 |
| CASH FLOWS FROM OPERATING ACTIVITIES: | | |
| Net loss | $(21,356) | $(12,631) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Depreciation and amortization | 1,012 | 660 |
| Equity-based compensation | 4,107 | 2,630 |
| Changes in operating assets and liabilities: | | |
| Accounts receivable | 3,005 | 4,011 |
| Prepaid expenses and other current assets | 1,205 | 704 |
| Accounts payable | 59 | (954) |
| Accrued expenses | (1,609) | (1,893) |
| Deferred revenue | (4,474) | (4,278) |
| Other assets | 318 | 268 |
| Other long-term liabilities | (37) | 85 |
| Net cash used in operating activities | (17,770) | (11,398) |
| CASH FLOWS FROM INVESTING ACTIVITIES: | | |
| Purchases of property and equipment | (1,850) | (4,162) |
| Net cash used in investing activities | (1,850) | (4,162) |
| CASH FLOWS FROM FINANCING ACTIVITIES: | | |
| Proceeds from options exercised | 6,720 | 47 |
| Net cash provided by financing activities | 6,720 | 47 |
| Net decrease in cash and cash equivalents | (12,900) | (15,513) |
| Cash and cash equivalents, beginning of period | 340,678 | 273,064 |
| Cash and cash equivalents, end of period | $327,778 | $257,551 |
| SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION: | | |
| Purchases of property and equipment unpaid at period end | $703 | $378 |

See notes to consolidated financial statements.

INTELLIA THERAPEUTICS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (UNAUDITED)

1. Overview and Basis of Presentation

Intellia Therapeutics, Inc. (collectively referred to with its wholly owned, controlled subsidiary, Intellia Securities Corp., as "Intellia" or the "Company") is a genome editing company focused on developing curative therapeutics utilizing a biological tool known as CRISPR/Cas9.

The consolidated financial statements of the Company included herein have been prepared, without audit, pursuant to the rules and regulations of the Securities and Exchange Commission ("SEC"). Certain information and footnote disclosures normally included in financial statements prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP") have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these consolidated financial statements should be read in conjunction with the financial statements and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2017.

The unaudited consolidated financial statements include the accounts of Intellia Therapeutics, Inc. and its wholly-owned, controlled subsidiary, Intellia Securities Corp. All intercompany balances and transactions have been eliminated in consolidation. The only item comprising comprehensive loss is net loss.

In the opinion of management, the information furnished reflects all adjustments, all of which are of a normal and recurring nature, necessary for a fair presentation of the results for the reported interim periods. The Company considers events or transactions that occur after the balance sheet date but before the financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The three months ended March 31, 2018 and 2017 are referred to as the first quarter of 2018 and 2017, respectively. The results of operations for interim periods are not necessarily indicative of results to be expected for the full year or any other interim period.

2. Summary of Significant Accounting Policies

Revenue Recognition

In May 2014, the Financing Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2014-09, Revenue from Contracts with Customers (Topic 606), which superseded existing revenue recognition guidance. The Company adopted ASU 2014-09 and its related amendments (collectively known as "ASC 606") on January 1, 2018 using the modified retrospective method. The reported results for 2018 reflect the application of ASC 606 guidance while the reported results for 2017 were prepared under the guidance of ASC 605, Revenue Recognition ("ASC 605" or "legacy GAAP"). The adoption of ASC 606 represents a change in accounting principle that will more closely align revenue recognition with the delivery of the Company's goods and services and will provide financial statement readers with enhanced disclosures.

In accordance with ASC 606, revenue is recognized when a customer obtains control of promised goods or services. The amount of revenue recognized reflects the consideration to which the Company expects to be entitled to receive in exchange for these goods and services. To achieve this core principle, the Company applies the following five steps:

1) Identify the contract with the customer

A contract with a customer exists when (i) the Company enters into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the related payment terms, (ii) the contract has commercial substance, and (iii) the Company determines that collection of substantially all consideration for goods and services that are transferred is probable based on the customer's intent and ability to pay the promised consideration. The Company applies judgment in determining the customer's intent and ability to pay, which is based on a variety of factors including the customer's historical payment experience, or in the case of a new customer, published credit and financial information pertaining to the customer.

2) Identify the performance obligations in the contract

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other available resources, and are distinct in the context of the contract, whereby the transfer of the good or service is separately identifiable from other promises in the contract. To the extent a contract includes multiple promised goods and services, the Company must apply judgment to determine whether promised goods and services are both capable of being distinct and distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.

3) Determine the transaction price

The transaction price is determined based on the consideration to which the Company will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, the Company estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method, depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in the Company's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Any estimates, including the effect of the constraint on variable consideration, are evaluated at each reporting period for any changes. Determining the transaction price requires significant judgment, which is discussed in further detail for each of the Company's collaboration agreements in Note 5. In addition, neither of the Company's contracts as of March 31, 2018 contained a significant financing component.

4) Allocate the transaction price to performance obligations in the contract

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. However, if a series of distinct services that are substantially the same qualifies as a single performance obligation in a contract with variable consideration, the Company must determine if the variable consideration is attributable to the entire contract or to a specific part of the contract. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis unless the transaction price is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation. The consideration to be received is allocated among the separate performance obligations based on relative standalone selling prices. The Company typically determines standalone selling prices using an adjusted market assessment approach model.

5) Recognize revenue when or as the Company satisfies a performance obligation

The Company satisfies performance obligations either over time or at a point in time. Revenue is recognized over time if either (i) the customer simultaneously receives and consumes the benefits provided by the entity's performance, (ii) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or (iii) the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer. Examples of control are using the asset to produce goods or services, enhance the value of other assets, or settle liabilities, and holding or selling the asset.

As of March 31, 2018, the Company's only revenue recognized is related to collaboration agreements with third parties. As discussed in further detail in Note 5, the Company enters into out-licensing agreements which are within the scope of ASC 606, under which it licenses certain rights to its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: nonrefundable, upfront fees; development, regulatory, and commercial milestone payments; research and development funding payments; and royalties on the net sales of licensed products. Each of these payments results in collaboration revenues, except for revenues from royalties on the net sales of licensed products, which are classified as royalty revenues.

Licenses of intellectual property: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from consideration allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the licenses. For

licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement that includes development milestone payments, the Company evaluates the probability of reaching the milestones and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur in the future, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received and therefore revenue recognized is constrained as management is unable to assert that a reversal of revenue would not be possible. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues and earnings in the period of adjustment.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on levels of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its collaboration agreements.

The Company receives payments from its customers based on billing schedules established in each contract. The Company’s contract liabilities consist of deferred revenue. Upfront payments and fees are recorded as deferred revenue upon receipt or when due, and may require deferral of revenue recognition to a future period until the Company performs its obligations under these arrangements.

The following table presents changes in the Company’s contract liabilities during the three months ended March 31, 2018 (in thousands):

| | Balance at Beginning of Period | Additions | Deductions | Balance at End of Period |
|---|---|---|---|---|
| Three months ended March 31, 2018 | | | | |
| Contract liabilities: | | | | |

| | | | | |
|---|---|---|---|---|
| Deferred revenue | $ 59,868 | $ 1,000 | $ (5,474) | $ 55,394 |

During the three months ended March 31, 2018, the Company recognized the following revenues as a result of changes in the contract liability balance (in thousands):

| Revenue recognized in the period from: | Three Months Ended March 31, 2018 |
|---|---|
| Amounts included in the contract liability at the beginning of the period | $ 5,474 |

The following table shows the impact of adoption to our consolidated statement of income and balance sheet:

| | Three Months Ended March 31, 2018 | | |
|---|---|---|---|
| | | Impact of changes in accounting policies | |
| | As Reported | Balances without adoption of ASC 606 | Effect of Change Higher/(Lower) |
| Collaboration revenue | $7,469 | $7,674 | $ (205) |
| Operating loss | (22,430) | (22,225) | (205) |
| Net loss | $(21,356) | $(21,151) | $ (205) |
| Net loss per share, basic and diluted | $(0.51) | $(0.50) | $ (0.01) |

| | March 31, 2018 | | |
|---|---|---|---|
| | | Impact of changes in accounting policies | |
| | As Reported | Balances without adoption of ASC 606 | Effect of Change Higher/(Lower) |
| Liabilities: | | | |
| Deferred revenue - current | $17,062 | $20,404 | $ (3,342) |
| Deferred revenue - noncurrent | 38,332 | 40,216 | (1,884) |
| Stockholders' equity: | | | |
| Accumulated deficit | $(137,038) | $(142,264) | $ 5,226 |

Costs to obtain and fulfill a contract

The Company did not incur any expenses to obtain collaboration agreements and costs to fulfill those contracts do not generate or enhance resources of the Company. As such, no costs to obtain or fulfill a contract have been capitalized in any period.

The Company has applied the new standard to all of its contracts.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASC 606, which superseded existing revenue recognition guidance. The standard’s core principle is that a company will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. The Company adopted ASC 606 effective on January 1, 2018 using the modified retrospective method. Please see the above “Revenue Recognition” section for a discussion of the Company’s updated policies related to

revenue recognition and accounting for costs to obtain and fulfill a customer contract.

Impact of Adoption

The Company adopted ASC 606 using the modified retrospective method. The cumulative effect of applying the new guidance to all contracts with customers that were not completed as of January 1, 2018 was recorded as an adjustment to accumulated deficit as of the adoption date. As a result of applying the modified retrospective method to adopt the new guidance, the following adjustments were made to accounts on the consolidated balance sheet as of January 1, 2018:

Consolidated Balance Sheet

| | January 1, 2018 (in thousands) | | |
|---|---|---|---|
| | Pre-Adoption | ASC 606 Adjustment | Post-Adoption |
| Current portion of deferred revenue | $21,188 | $ (2,769) | $ 18,419 |
| Deferred revenue, net of current portion | 44,111 | (2,662) | 41,449 |
| Accumulated deficit | (121,113) | 5,431 | (115,682) |

In February 2016, the FASB issued ASU No. 2016-02, Leases ("ASU 2016-02"). ASU 2016-02 amends ASC 840, Leases, by introducing a lessee model that requires balance sheet recognition of most leases. The Company is the lessee under certain leases that are accounted for as operating leases. The proposed changes would require that substantially all of the Company's operating leases be recognized as assets and liabilities on the Company's balance sheet. ASU 2016-02 will be effective for the Company for annual periods, and interim periods within those annual periods, beginning January 1, 2019. The Company is evaluating the impact that the adoption of ASU 2016-02 will have on its consolidated financial statements but expects that the Company will recognize a significant lease obligation upon adoption.

3. Fair Value Measurements

The Company classifies fair value based measurements using a three-level hierarchy that prioritizes the inputs used to measure fair value. This hierarchy requires entities to maximize the use of observable inputs and minimize the use of unobservable inputs. The three levels of inputs used to measure fair value are as follows: Level 1, quoted market prices in active markets for identical assets or liabilities; Level 2, observable inputs other than quoted market prices included in Level 1, such as quoted market prices for markets that are not active or other inputs that are observable or can be corroborated by observable market data; and Level 3, unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities, including certain pricing models, discounted cash flow methodologies and similar techniques that use significant unobservable inputs.

The Company's financial instruments as of March 31, 2018 and December 31, 2017 consisted primarily of cash and cash equivalents, accounts receivable and accounts payable. As of March 31, 2018 and December 31, 2017, the Company's financial assets recognized at fair value on a recurring basis consisted of the following:

| | Fair Value as of March 31, 2018 | | | |
|---|---|---|---|---|
| | Total | Level 1 | Level 2 | Level 3 |
| | (In thousands) | | | |
| Cash equivalents | $313,960 | $313,960 | $ — | $ — |
| Total | $313,960 | $313,960 | $ — | $ — |

| | Fair Value as of December 31, 2017 | | | |
|---|---|---|---|---|
| | Total | Level 1 | Level 2 | Level 3 |
| | (In thousands) | | | |
| Cash equivalents | $330,896 | $330,896 | $ — | $ — |
| Total | $330,896 | $330,896 | $ — | $ — |

The Company estimates the fair value of its cash equivalents using quoted market prices in active markets. Other financial instruments, including accounts receivable and accounts payable, are carried at cost, which approximate fair value due to the short duration and term to maturity.

4. Accrued Expenses

Accrued expenses consisted of the following:

| | March 31, 2018 | December 31, 2017 |
|---|---|---|
| | (In thousands) | |
| Employee compensation and benefits | $2,760 | $ 4,773 |
| Research and development and professional expenses | 3,845 | 3,226 |
| Accrued expenses | $6,605 | $ 7,999 |

5. Collaborations

Novartis Institutes for BioMedical Research

In December 2014, the Company entered into a strategic collaboration agreement (the "Novartis Agreement") with Novartis Institutes for Biomedical Research, Inc. ("Novartis"), primarily focused on the development of new ex vivo CRISPR/Cas9-based therapies using chimeric antigen receptor T cells ("CAR-T cells") and hematopoietic stem cells ("HSCs").

Agreement Structure

Under the terms of the collaboration, the Company and Novartis may research potential therapeutic, prophylactic and palliative ex vivo applications of the CRISPR/Cas9 technology in HSCs and CAR-T cells. The Company and Novartis agreed to conduct research of HSC targets under a research plan agreed upon by both parties. Within the HSC therapeutic space, Novartis may obtain exclusive rights to a limited number of these HSC targets, to be selected by Novartis in a series of selection windows, the last of which closes 90 days before the fifth anniversary of the effective date of the Novartis Agreement. The Company has the right to choose a limited number of HSC targets for its exclusive development and commercialization per the specified selection schedule. Following these selections by Novartis and the Company, Novartis may obtain rights to research an additional limited number of HSC targets on a non-exclusive basis. If Novartis does not exercise its selection rights within each selection window, any such rights will be deemed forfeited by Novartis. Novartis is required to use commercially reasonable efforts to research, develop and commercialize a specified number of HSC products directed to each of their selected HSC targets.

The Company also agreed to collaborate with Novartis on research activities for CAR-T cell targets pursuant to a CAR-T cell program research plan approved by the CAR-T cell subcommittee of the collaboration's joint steering committee. After completion of the activities contemplated by the CAR-T cell program research plan, Novartis will assume sole responsibility for developing any products arising from that research plan and will be responsible for additional costs and expenses of developing, manufacturing and commercializing its selected research targets. Novartis is required to use commercially reasonable efforts to research, develop or commercialize at least one CAR-T cell product directed to each of its selected CAR-T cell targets. In the last two years of the five-year collaboration term, Novartis will have the option to select a limited number of targets for research, development and commercialization of in vivo therapies using the Company's CRISPR/Cas9 platform, on a non-exclusive basis. Following Novartis' selection of each in vivo target, Novartis may offer the Company the right to participate in the research and development of such targets, in which case an in vivo program research plan for such target will be entered into between the Company and Novartis. Novartis is required to use commercially reasonable efforts to research, develop or commercialize at least one in vivo product directed to each of its selected targets. Novartis' in vivo target selections are subject to certain restrictions, including that the targets, or all targets within a limited number of organs: (i) have not already been reserved by the Company pursuant to our limited right to do so under the agreement; (ii) are not the subject of a collaboration or pending collaboration with a third party; and (iii) are not the subject of ongoing or planned research and development by the Company.

The Company received an upfront technology access payment from Novartis of $10.0 million in January 2015 and is entitled to additional technology access fees of $20.0 million and quarterly research payments of $1.0 million, or up to $20.0 million in the aggregate, during the five-year research term. For each product under the collaboration, subject to certain conditions, the Company may be eligible to receive (i) up to $30.3 million in development milestones, including for the filing of an investigational new drug ("IND") application and for the dosing of the first patient in each of Phase IIa, Phase IIb and Phase III clinical trials, (ii) up to $50.0 million in regulatory milestones for the product's first indication, including regulatory approvals in the U.S. and European Union ("EU"), (iii) up to $50.0 million in regulatory milestones for the product's second indication, if any, including U.S. and EU regulatory approvals, (iv) royalties on net sales in the mid-single digits, and (v) net sales milestone payments of up to $100.0 million. The

Company may also be eligible to receive payments for: (i) each additional HSC target selected by Novartis beyond its initial defined allocation, (ii) each in vivo target that Novartis selects and (iii) any exercise by Novartis of certain license options under the Novartis Agreement. Additionally, at the inception of the arrangement, Novartis invested $9.0 million to purchase the Company's Class A-1 and Class A-2 Preferred Units under a Unit Purchase Agreement (the "Unit Purchase Agreement"). The Company considered whether the Unit Purchase Agreement would be subject to combination with the Novartis Agreement and determined that they should be combined because the terms of these arrangements are closely interrelated and were negotiated contemporaneously. The Unit Purchase Agreement and the Novartis Agreement are collectively referred to herein as the "Novartis Arrangement".

The Company assessed the Novartis Arrangement in accordance with ASC 606. The Company evaluated the promised goods and services under the Novartis Arrangement and determined that the Novartis Arrangement included two performance obligations: (1) a combined performance obligation representing a series of distinct goods and services including the licenses to research, develop and commercialize HSC products and their associated research activities and the licenses to research, develop and commercialize CAR-T cell products and their associated research activities; and (2) the preferred units.

Under the Novartis Arrangement, the Company determined that the transaction price was $59.0 million consisting of the following consideration: (1) the upfront technology access payment of $10.0 million; (2) the additional technology access fees of $20.0 million; (3) the Company's estimate of variable consideration of $20.0 million related to the quarterly research payments; and (4) the payment for the preferred units of $9.0 million. None of the clinical or regulatory milestones were included in the transaction price, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon future regulatory progress and the licensee's efforts. Any consideration related to sales-based milestones and royalties will be recognized when the related sales occur as they were determined to relate predominantly to the licenses granted to Novartis and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and when events whose outcomes are resolved or other changes in circumstances occur.

The Company first allocated $11.6 million of the transaction price to the preferred units to record the preferred units purchased by Novartis at fair value. The Company then allocated the remaining $47.4 million of the transaction price to the remaining combined performance obligation of the licenses and associated research activities for HSC and CAR-T cell products. Revenue allocated to the combined performance obligation of the licenses and associated research activities for HSC and CAR-T cell products is being recognized on a straight-line basis over a period of five years, which, in management's judgment, is the best measure of progress towards satisfying the performance obligation and represents the Company's best estimate of the period of the obligation.

Collaboration Revenue

Through March 31, 2018, excluding amounts allocated to Novartis' purchase of the Company's Class A-1 and Class A-2 Preferred Units, the Company had recorded a total of $35.4 million in cash and accounts receivable under the Novartis Arrangement. Through March 31, 2018, the Company has recognized $30.9 million of collaboration revenue, including $2.4 million and $2.2 million during the three months ended March 31, 2018 and 2017, respectively. As of March 31, 2018, there was approximately $16.4 million of the aggregate transaction price remaining to be recognized, which will be recognized through December 2019.

As of March 31, 2018 and December 31, 2017, the Company had accounts receivable of $1.0 million and $6.0 million, respectively, related to this agreement. As of March 31, 2018 and December 31, 2017, the Company had deferred revenue of $4.4 million and $11.2 million, respectively, related to this agreement. Amounts for 2018 are reflective of accounting under ASC 606 and amounts for 2017 are reflective of accounting under ASC 605 and therefore may not be comparable.

Regeneron Pharmaceuticals, Inc.

In April 2016, the Company entered into a license and collaboration agreement (the "Regeneron Agreement") with Regeneron Pharmaceuticals, Inc. ("Regeneron"). The agreement includes a product component to research, develop and commercialize CRISPR/Cas-based therapeutic products primarily focused on genome editing in the liver as well as a technology collaboration component, pursuant to which the Company and Regeneron will engage in research and development activities aimed at discovering and developing novel technologies and improvements to CRISPR/Cas

technology to enhance the Company's gene editing platform. Under this agreement, the Company also may access the Regeneron Genetics Center and proprietary mouse models to be provided by Regeneron for a limited number of the Company's liver programs.

Agreement Structure

Under the terms of the collaboration, the Company and Regeneron have agreed to a target selection process, whereby Regeneron may obtain exclusive rights for up to 10 targets to be chosen by Regeneron during the collaboration term, subject to various adjustments and limitations set forth in the agreement. Of these 10 total targets, Regeneron may select up to five non-liver targets, while the remaining targets must be focused in the liver. At the inception of the agreement, Regeneron selected the first of its 10 targets, which will be subject to a co-development and co-commercialization arrangement between the Company and Regeneron.

The Company retains the exclusive right to solely develop products for certain indications. During the target selection process, the Company has the right to choose additional liver targets for its own development using commercially reasonable efforts. Certain targets that either the Company or Regeneron select may be subject to further co-development and co-commercialization arrangements at the Company's or Regeneron's option, as applicable, which either can exercise pursuant to defined conditions. In addition, subject to certain restrictions, Regeneron will be able to replace a limited number of targets with substitute targets upon the payment of a specified replacement fee, in which case exclusive rights to the replaced target revert to the Company. Regeneron's target selections are subject to certain additional restrictions, including that non-liver targets are not the subject of ongoing or planned research and development by the Company or are not the subject of a collaboration or pending collaboration with a third party.

Research activities under the collaboration will be governed by evaluation and research and development plans that will outline the parties' responsibilities under, anticipated timelines of and budgets for, the various programs. The Company will assist Regeneron with the preliminary evaluation of liver targets, and Regeneron will be responsible for preclinical research and the conduct of clinical development, manufacturing and commercialization of products directed to each of its exclusive targets under the oversight of a joint steering committee. The Company may assist, as requested by Regeneron, with the later discovery and research of product candidates directed to any selected target. For each selected target, Regeneron is required to use commercially reasonable efforts to submit regulatory filings necessary to achieve IND acceptance for at least one product directed to each applicable target, and following IND acceptance for at least one product, to develop and commercialize such product.

In connection with this collaboration, Regeneron agreed to purchase $50.0 million of the Company's common stock in a private placement under a Stock Purchase Agreement (the "Stock Purchase Agreement") concurrent with the Company's initial public offering, and the Company received a nonrefundable upfront payment of $75.0 million. In addition, the Company is eligible to earn, on a per-licensed target basis, (i) up to $25.0 million in development milestones, including for the dosing of the first patient in each of Phase I, Phase II and Phase III clinical trials, (ii) up to $110.0 million in regulatory milestones, including for the acceptance of a regulatory filing in the U.S., and U.S. and ex-U.S. regulatory approvals, and (iii) up to $185.0 million in sales-based milestone payments. The Company is also eligible to earn royalties ranging from the high single digits to low teens, in each case, on a per-product basis, which royalties are potentially subject to various reductions and offsets and are further subject to the Company's existing low- to mid-single-digit royalty obligations under a license agreement with Caribou Biosciences, Inc. ("Caribou"). In addition, Regeneron is obligated to fund 50.0 percent of the research and development costs for the transthyretin amyloidosis program, the first target selected by Regeneron, which will be subject to a co-development and co-commercialization arrangement between the Company and Regeneron.

The Company considered whether the Stock Purchase Agreement would be subject to combination with the Regeneron Agreement and determined that they should be combined because the terms of these arrangements are closely interrelated and were negotiated contemporaneously. The Stock Purchase Agreement and the Regeneron Agreement are collectively referred to herein as the "Regeneron Arrangement".

The Company assessed the Regeneron Arrangement in accordance with ASC 606. The Company evaluated the promised goods and services under the Regeneron Arrangement and determined that the Regeneron Arrangement included three performance obligations: (1) a combined performance obligation including the licenses to targets and the associated research activities and evaluation plans; (2) a combined performance obligation including the technology collaboration and associated research activities; and (3) the common stock.

Under the Regeneron Arrangement, the Company determined that the transaction price was $125.0 million, consisting of the following consideration: (1) the nonrefundable upfront payment of $75.0 million; and (2) the payment for the common stock of $50.0 million. None of the clinical or regulatory milestones were included in the transaction price, as all milestone amounts were fully constrained. As part its evaluation of the constraint, the Company considered

numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future regulatory progress and the licensee's efforts. Any consideration related to sales-based milestones and royalties will be recognized when the related sales occur as they were determined to relate predominantly to the licenses granted to Regeneron and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and when events whose outcome are resolved or other changes in circumstances occur.

The Company first allocated $50.0 million of the transaction price to the common stock. The common stock was sold at its standalone selling price and the Company concluded that the total discount inherent in the arrangement is entirely attributable to the combined performance obligation including the licenses to targets and associated research activities and evaluation plans and the combined performance obligation including the technology collaboration and associated research activities. As such, the remaining $75.0 million of the transaction price was allocated to the combined performance obligation including the licenses to targets and associated research activities and evaluation plans and the combined performance obligation including the technology collaboration and associated research activities on a relative standalone selling price basis. The Company estimated the standalone selling price of each combined performance obligation by taking into consideration internal estimates of research and development personnel needed to perform the research and development services, estimates of expected cash outflows to third parties for services and supplies, selling prices of comparable transactions and typical gross profit margins. As a result of this evaluation, the Company allocated $63.8 million to the combined performance obligation including the licenses to targets and associated research activities and evaluation plans and $11.2 million to the combined performance obligation including the technology collaboration and associated research activities. The $63.8 million allocated to the combined performance obligation including the licenses to targets and associated research activities and evaluation plans is being recognized on a straight-line basis over the six-year performance period of the arrangement, which, in management's judgment, is the best measure of progress towards satisfying the performance obligation and represents the Company's best estimate of the period of the obligation. The $11.2 million allocated to the combined performance obligation including the technology collaboration and associated research activities is being recognized on a straight-line basis over a period beginning with the inception of the technology collaboration in September 2016 through the end of the arrangement, which, in management's judgment, is the best measure of progress towards satisfying the performance obligation and represents the Company's best estimate of the period of the obligation.

Collaboration Revenue

Through March 31, 2018, excluding the amounts allocated to Regeneron's purchase of common stock, the Company recorded a $75.0 million upfront payment and $6.6 million for research and development services under the Regeneron Arrangement. Through March 31, 2018, the Company has recognized $30.6 million of collaboration revenue, including $5.1 million and $4.1 million during the three months ended March 31, 2018 and 2017, respectively, in the consolidated statements of operations related to this arrangement. As of March 31, 2018, there was approximately $51.0 million of the aggregate transaction price remaining to be recognized, which will be recognized ratably through April 2022.

As of March 31, 2018 and December 31, 2017, the Company had deferred revenue of $51.0 million and $54.1 million, respectively, and accounts receivable of $6.5 million and $4.5 million, respectively, related to this arrangement.

Agreement Termination Rights

The collaboration term ends in April 2022, except that Regeneron may make a one-time payment of $25.0 million to extend the term for an additional two-year period. The agreement will continue until the date when no royalty or other payment obligations are due, unless earlier terminated in accordance with the terms of the agreement. Regeneron's royalty payment obligations expire on a country-by-country and product-by-product basis upon the later of (i) the expiration of the last valid claim of the royalty-bearing patents covering such product in such country, (ii) 12 years from the first commercial sale of such product in such country, or (iii) the expiration of regulatory exclusivity for such product. The Company may terminate the agreement on a target-by-target basis if Regeneron or any of its affiliates institutes a patent challenge against the Company's CRISPR/Cas or certain other background patent rights. The Company may also terminate the agreement on a target-by-target basis if Regeneron does not proceed with the development of a product directed to a selected target within specified periods of time. Regeneron may terminate the agreement, without cause, upon 180 days written notice to the Company, either in its entirety or on a target-by-target

basis, in which event, certain rights in the terminated targets and associated intellectual property revert to the Company, as described in the agreement. Following such termination, the Company may owe Regeneron royalties, in certain circumstances, up to mid-single digits on any terminated targets that the Company subsequently commercializes on a product-by-product basis for a period of 12 years after the first commercial sale of any such products. Either party may terminate the agreement either in its entirety or with respect to the technology collaboration or one or more of the targets selected by Regeneron, in the event of the other party's uncured material breach.

6. Equity-Based Compensation

Equity-based compensation expense is classified in the consolidated statements of operations as follows:

| | Three Months Ended March 31, | |
|---|---|---|
| | 2018 | 2017 |
| | (In thousands) | |
| Research and development | $2,393 | $1,503 |
| General and administrative | 1,714 | 1,127 |
| Total | $4,107 | $2,630 |

Restricted Stock

The following table summarizes the Company's restricted stock activity for the three months ended March 31, 2018:

| | Number of Shares | Weighted Average Grant Date Fair Value per Share |
|---|---|---|
| Unvested restricted stock as of January 1, 2018 | 479,822 | $ 0.90 |
| Granted | 71,875 | 23.46 |
| Vested | (149,846) | 0.78 |
| Cancelled | (2,022) | 1.34 |
| Unvested restricted stock as of March 31, 2018 | 399,829 | $ 5.02 |

As of March 31, 2018, there was $3.3 million of unrecognized equity-based compensation expense related to restricted stock that is expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 1.7 years.

Stock Options

The weighted average grant date fair value of options, estimated as of the grant date using the Black-Scholes option pricing model, was $18.28 per option and $10.38 per option for those options granted during the three months ended March 31, 2018 and 2017, respectively. Key assumptions used to apply this pricing model were as follows:

| | Three Months Ended March 31, 2018 | | Three Months Ended March 31, 2017 | |
|---|---|---|---|---|
| Risk-free interest rate | 2.5 | % | 1.9 | % |
| Expected life of options | 6.0 years | | 6.0 years | |
| Expected volatility of underlying stock | 89.4 | % | 92.6 | % |
| Expected dividend yield | 0.0 | % | 0.0 | % |

The following is a summary of stock option activity for the three months ended March 31, 2018:

| | Number of Options | Weighted Average Exercise Price per Share | Weighted Average Remaining Contractual Term (In years) | Aggregate Intrinsic Value (In thousands) |
|---|---|---|---|---|
| Outstanding at January 1, 2018 | 4,705,448 | $ 12.09 | | |
| Granted | 792,414 | 24.44 | | |
| Exercised | (709,321) | 9.47 | | |
| Forfeited | (17,224) | 14.62 | | |
| Outstanding at March 31, 2018 | 4,771,317 | $ 14.52 | 8.68 | $ 35,070 |
| Exercisable at March 31, 2018 | 1,343,841 | $ 9.64 | 7.95 | $ 15,420 |

As of March 31, 2018, there was $39.2 million of unrecognized compensation cost related to stock options that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 3.1 years.

7. Loss Per Share

The Company calculates basic (loss) earnings per share by dividing (loss) income allocable to common stockholders by the weighted average number of common shares outstanding. The Company computes diluted (loss) earnings per share after giving consideration to the dilutive effect of stock options and unvested restricted stock that are outstanding during the period, except where such securities would be anti-dilutive.

Basic and diluted loss per share attributable to common stockholders was calculated as follows:

| | Three Months Ended March 31, | |
|---|---|---|
| | 2018 | 2017 |
| | (In thousands) | |
| Net loss | $(21,356) | $(12,631) |
| Weighted average shares outstanding, basic and diluted | 42,043 | 34,723 |
| Net loss per share attributable to common stockholders, basic and diluted | $(0.51) | $(0.36) |

The following common stock equivalents were excluded from the calculation of diluted loss per share because their inclusion would have been anti-dilutive:

| | Periods Ended March 31, | |
|---|---|---|
| | 2018 | 2017 |
| | (In thousands) | |
| Unvested restricted stock | 400 | 1,175 |
| Stock options | 4,771 | 4,373 |
| Total | 5,171 | 5,548 |

8. Related Party Transactions

Caribou Therapeutics

In July 2014, the Company issued Caribou Therapeutics Holdco, LLC, a wholly-owned subsidiary of Caribou, 8,110,599 Junior Preferred Units. As a result of this and related transactions, Caribou owned 9.3 percent of the Company's voting interests as of March 31, 2018.

The Company recognized general and administrative expense of $0.2 million during the three months ended March 31, 2018, and a de minimis amount during the three months ended March 31, 2017, related to the Company's obligation to pay 30.0 percent of Caribou's patent prosecution, filing and maintenance costs.

Novartis Institutes for BioMedical Research

In connection with its entry into the collaboration and license agreement and related equity transactions with Novartis, the Company issued Novartis 4,761,905 Class A-1 Preferred Units and 2,666,666 Class A-2 Preferred Units. In August 2015, Novartis acquired 761,905 shares of the Company's Series B Preferred Stock, and in May 2016, Novartis acquired 277,777 shares of the Company's common stock in a private placement transaction concurrent with the Company's IPO. As a result of these and subsequent transactions, Novartis collectively owned 9.9% of the Company's voting interests as of March 31, 2018.

The Company recognized collaboration revenue of $2.4 million and $2.2 million during the three months ended March 31, 2018 and 2017, respectively, in the consolidated statements of operations related to this agreement. As of March 31, 2018 and December 31, 2017, the Company had recorded accounts receivable of $1.0 million and $6.0 million and deferred revenue of $4.4 million and $11.2 million, respectively, related to this collaboration. Refer to Note 5, Collaborations, for additional information regarding this collaboration agreement.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

Forward-looking Information

This Quarterly Report on Form 10-Q contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements may be identified by such forward-looking terminology as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the these terms or other comparable terminology. Our forward-looking statements are based on a series of expectations, assumptions, estimates and projections about our company, are not guarantees of future results or performance and involve substantial risks and uncertainty. We may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. Our business and our forward-looking statements involve substantial known and unknown risks and uncertainties, including the risks and uncertainties inherent in our statements regarding:

- the initiation, timing, progress and results of our research and development programs and future preclinical and clinical studies;
- our ability to apply a risk-mitigated strategy to efficiently discover and develop product candidates, including by applying learnings from one program to other programs;
- our ability to create or maintain a pipeline of product candidates;
- our ability to manufacture or obtain material for our product candidates;
- our ability to advance any product candidates into, and successfully complete, clinical studies;
- our ability to advance our therapeutic delivery capabilities;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to operate, including commercializing products, without infringing the proprietary rights of others;
- the issuance of regulatory guidance regarding preclinical and clinical studies for genome editing products;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the potential benefits of strategic collaboration agreements and our ability to enter into strategic arrangements;
- our ability to maintain and establish collaborations and licenses or obtain additional funding;
- our financial performance;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under the caption "Risk Factors."

All of our forward-looking statements are as of the date of this Quarterly Report on Form 10-Q only. In each case, actual results may differ materially from such forward-looking information. We can give no assurance that such expectations or forward-looking statements will prove to be correct. An occurrence of or any material adverse change in one or more of the risk factors or risks and uncertainties referred to in this Quarterly Report on Form 10-Q or included in our other public disclosures or our other periodic reports or other documents or filings filed with or furnished to the Securities and Exchange Commission (the "SEC") could materially and adversely affect our business, prospects, financial condition and results of operations. Except as required by law, we do not undertake or plan to update or revise any such forward-looking statements to reflect actual results, changes in plans, assumptions, estimates or projections or other circumstances affecting such forward-looking statements occurring after the date of this Quarterly Report on Form 10-Q, even if such results, changes or circumstances make it clear that any forward-looking information will not be realized. Any public statements or disclosures by us following this Quarterly Report on Form 10-Q that modify or impact any of the forward-looking statements contained in this Quarterly Report on Form 10-Q will be deemed to modify or supersede such statements in this Quarterly Report on Form 10-Q.

Management Overview

Intellia Therapeutics, Inc. ("we," "us," "our," "Intellia," or the "Company") was formed in 2014 and is a leading genome editin company focused on the development of proprietary, curative therapeutics utilizing a biological tool known as CRISPR/Cas9. We believe that the CRISPR/Cas9 technology has the potential to transform medicine by permanently editing disease-associated genes or genetic material in the human body with a single treatment course, and via cell therapies that can replace a patient's diseased cells or by using engineered immune cells to better treat cancer and immunological diseases. We intend to leverage our leading scientific expertise, clinical development experience and intellectual property ("IP") position to unlock broad therapeutic applications of CRISPR/Cas9 genome editing and develop new therapeutic products.

Our management's discussion and analysis of our financial condition and results of operations are based upon our unaudited consolidated financial statements included in this Quarterly Report on Form 10-Q, which have been prepared by us in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"), for interim periods and with Regulation S-X promulgated under the Securities Exchange Act of 1934, as amended. This discussion and analysis should be read in conjunction with these unaudited consolidated financial statements and the notes thereto included elsewhere in this Quarterly Report on Form 10-Q as well as in conjunction with the audited financial statements and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2017.

We commenced active operations in mid-2014, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical research and studies and evaluating a clinical path for our pipeline programs. To date, we have financed our operations primarily through our collaborations with Novartis Institutes for BioMedical Research, Inc., ("Novartis"), and Regeneron Pharmaceuticals, Inc., ("Regeneron"), our initial public offering and private placements of our common and preferred stock. All of our revenue to date has been collaboration revenue. Since our inception and through March 31, 2018, we have raised an aggregate of approximately $508.6 million to fund our operations, of which $112.1 million was through our collaboration agreements, $170.5 million was from our initial public offering and concurrent private placements, $141.0 million was from a secondary offering and $85.0 million was from the sale of convertible preferred stock.

We believe our product focus, therapeutic discovery and development strength, delivery expertise and intellectual property portfolio make us well-positioned to translate the potential of the CRISPR/Cas9 system into clinically meaningful genome editing-based therapeutics. To maximize our opportunity to rapidly develop clinically successful products, we are applying a risk-mitigating approach with our initial indications. Our approach is defined by four

primary criteria: (i) the type of edit—knockout, repair or insertion; (ii) the delivery modality for in vivo and ex vivo applications; (iii) the presence of established therapeutic endpoints; and (iv) the potential for the CRISPR/Cas9 system to provide therapeutic benefits when compared to existing therapeutic modalities. Our initial indications include in vivo programs focused on diseases attributable to genes expressed in the liver that have significant unmet medical needs – transthyretin amyloidosis, which we are co-developing with Regeneron, alpha-1 antitrypsin deficiency, inborn errors of metabolism, including primary hyperoxaluria, and chronic hepatitis B infection – as well as ex vivo applications of the technology in chimeric antigen receptor T cell ("CAR-T cell") and hematopoietic stem cell ("HSC"), product candidates which are selectively partnered with our collaborator Novartis.

The following table illustrates our discovery programs and opportunities as of February 28, 2018:

In September 2017, we presented data from our completed long-term, 52-week mouse study, to evaluate the durability of in vivo genome editing following a single, intravenous administration of CRISPR/Cas9. With a single dose, we achieved and maintained an approximately 97 percent reduction in serum transthyretin amyloidosis target gene ("TTR") protein levels through 12 months. This sustained TTR reduction was caused by approximately 70 percent editing at the target DNA site in the liver. The treatment was well-tolerated at the time of administration and no adverse events were noted throughout the 52 weeks of follow-up study. These mouse durability results followed our presentation in August 2017 of initial data from rat studies demonstrating in vivo genome editing after a single, intravenous administration of CRISPR/Cas9. Across other studies we confirmed that our lipid nanoparticle ("LNP") system is transiently present with 99 percent clearance of messenger RNA ("mRNA") within 6 hours and of single guide RNA ("sgRNA") within 24 hours in the liver. In our August 2017 presentation, we reported that, using our LNP system in rats, we had observed up to 91 percent reduction in serum TTR protein levels and up to 66 percent editing at the target DNA site in the subject animals.

In October 2017, we released interim top-line data regarding our in vivo non-human primate ("NHP") exploratory pre-clinical studies. Specifically, based on preliminary studies currently at varying points of progress, liver genome editing rates using CRISPR/Cas9 delivered via our proprietary LNP system have ranged from 0.10 percent up to 32 percent after a single dose with various exploratory NHP guide RNAs ("gRNA"), LNP formulations and dosing regimens as well as with exploratory human cross-reactive gRNAs. In NHPs redosed with a subsequent application of our LNP formulations, we observed further editing that surpassed those levels achieved after a single dose, with multiple animals achieving a total of over 20 percent liver genome editing after a second dose.

These NHP results were similar to the results we observed in our initial rodent studies. We are conducting further optimization of our delivery system and proceeding to human guide selection. We expect to achieve higher levels of editing and reductions in serum levels of TTR protein as we achieved when we optimized the delivery system and CRISPR/Cas9 cargo used in our rodent models. We have begun investigational new drug ("IND")-enabling activities for a human therapeutic and we plan to initiate IND-enabling studies in mid-2018. We anticipate submitting an IND application for our lead indication, transthyretin amyloidosis, by the end of 2019.

To date, in both single and repeat dose experiments, our proprietary LNP delivery system has been well-tolerated with both NHP-specific gRNA and exploratory human cross-reactive gRNAs, as assessed by gross observation of the animals, clinical chemistry, hematology, and cytokine and complement levels. We are also encouraged by the reduction in serum TTR protein levels shown to date in animals with the highest levels of editing. We are conducting additional studies in multiple animal models to maximize editing rates through repeat dosing and formulation optimization.

In October 2017, we presented data from an in vivo mouse study showing, after a single intracerebral injection, delivery to the brain of one of our proprietary LNP formulations as demonstrated by the expression of tdTomato protein. Additionally, we presented data from another in vivo mouse study showing genome editing in brain tissue following single intracerebral injections of several proprietary LNP formulations. Editing was assessed under various dosing regimens with six different proprietary LNP formulations following a single intracerebral injection targeting the striatum and cerebellum. Under these various conditions, editing levels from less than 1 percent up to 28 percent were achieved in the striatal and cerebellar tissue. The injections were well tolerated and the mice did not display any behavioral changes post dosing.

In December 2017, we and our collaborator Novartis shared initial data from our research collaboration on genome-edited human HSCs. These data showed successful ex vivo editing of the erythroid specific enhancer region of BCL11A, a gene associated with ameliorating sickle cell disease, and the ability of these cells to steadily engraft in mice while maintaining their desired properties. Specifically, the data showed that greater than 80 percent target site modification in HSCs and progenitor CD34+ cells was achieved following electroporation of ribonucleoprotein ("RNP") composed of Cas9 and a gRNA selected for efficacy and potency. In addition, we demonstrated an approximately 40 percent reduction in BCL11A mRNA with a corresponding two-fold increase in -globin transcript and 30-40 percent more fetal hemoglobin-positive cells above background. Editing of CD34+ cells from patient donors resulted in similar decreases in BCL11A mRNA and increases in -globin transcript. We also showed engraftment over 16 weeks following transplantation of edited human bone marrow CD34+ cells into immune compromised mice, while maintaining editing levels in engrafted cells. We did not observe any off-target events in CD34+ cells edited with the selected gRNA, as measured by targeted next generation sequencing of sites identified through in silico prediction and based on an unbiased, genome-wide, oligo-insertion detection method.

Collaborations

Novartis

In December 2014, we entered into a strategic collaboration agreement with Novartis, primarily focused on the development of new ex vivo CRISPR/Cas9-based therapies using CAR-T cells and HSCs.

Agreement Structure

Under the terms of the collaboration, we and Novartis may research potential therapeutic, prophylactic and palliative ex vivo applications of our CRISPR/Cas9 technology in HSCs and CAR-T cells. We and Novartis agreed to conduct research of HSC targets under a research plan agreed upon by both parties. Within the HSC therapeutic space, Novartis may obtain exclusive rights to a limited number of these HSC targets, to be selected by Novartis in a series of selection windows. We have the right to choose a limited number of HSC targets for our exclusive development and commercialization per the specified selection schedule. Following these selections by Novartis and us, Novartis may obtain rights to research an additional limited number of HSC targets on a non-exclusive basis. Novartis is required to use commercially reasonable efforts to research, develop, and commercialize a specified number of HSC products directed to each of their selected HSC targets.

We have also agreed to collaborate with Novartis on research activities for CAR-T cell targets pursuant to the CAR-T cell program research plan approved by the CAR-T cell subcommittee of the collaboration's joint steering committee. After completion of the activities contemplated by the CAR-T cell program research plan, Novartis will assume sole responsibility for developing any products arising from that research plan and the costs and expenses of developing, manufacturing and commercializing its selected research targets. Novartis is required to use commercially reasonable efforts to research, develop or commercialize at least one CAR-T cell product directed to each of its selected CAR-T cell targets.

Starting in December 2017 and through the end of the collaboration in December 2019, Novartis has the option to select a limited number of targets for research, development and commercialization of in vivo therapies using our CRISPR/Cas9 platform, on a non-exclusive basis. Following Novartis' selection of each in vivo target, Novartis may offer us the right to participate in the research and development of such targets, in which case an in vivo program research plan for such target will be entered into between us and Novartis. Novartis is required to use commercially reasonable efforts to research, develop and commercialize at least one in vivo product directed to each of its selected in vivo targets. Novartis' in vivo target selections are subject to certain restrictions, including that the targets, or all targets within a limited number of organs: (i) have not already been reserved by us pursuant to our limited right to do so under the agreement; (ii) are not the subject of a collaboration or pending collaboration with a third party; and (iii) are not the subject of ongoing or planned research and development by us.

Under the agreement, we received an upfront technology access payment of $10.0 million and are entitled to additional technology access fees of $20.0 million and quarterly research payments of $1.0 million, or up to $20.0 million in the aggregate, during the five-year research term. In addition, for each product under the collaboration, subject to certain conditions, we may be eligible to receive (i) up to $30.3 million in development milestones, including for the filing of an IND application and for the dosing of the first patient in each of Phase IIa, Phase IIb and Phase III clinical trials, (ii) up to $50.0 million in regulatory milestones for the product's first indication, including regulatory approvals in the U.S., and the European Union ("EU"), (iii) up to $50.0 million in regulatory milestones for the product's second indication, if any, including U.S. and EU regulatory approvals, (iv) royalties on net sales in the mid-single digits, and (v) net sales milestone payments of up to $100.0 million. We may also be eligible to receive payments for: (i) each additional HSC target selected by Novartis beyond its initial defined allocation, (ii) each in vivo target that Novartis selects and (iii) any exercise by Novartis of certain license options under the agreement. Additionally, at the inception of the arrangement, Novartis invested $9.0 million to purchase our Class A-1 and Class A-2 Preferred Units. The difference between the cash proceeds received from Novartis for the units and the $11.6 million estimated fair value of those units at the date of issuance was determined to be $2.6 million. Accordingly, $2.6 million of the upfront technology access payment was allocated to record the preferred units purchased by Novartis at fair value.

Collaboration Revenue

Through March 31, 2018, excluding amounts allocated to Novartis' purchase of our Class A-1 and Class A-2 Preferred Units, we had recorded a total of $35.4 million in cash and accounts receivable under the Novartis agreement. Through March 31, 2018, we have recognized $30.9 million of collaboration revenue, including $2.4 million and $2.2 million during the three months ended March 31, 2018 and 2017, respectively, in the consolidated statements of operations related to this agreement. As of March 31, 2018 and December 31, 2017, we had accounts receivable of $1.0 million and $6.0 million, respectively, related to this agreement. As of March 31, 2018 and December 31, 2017, we had deferred revenue of $4.4 million and $11.2 million, respectively, related to this agreement.

Regeneron

In April 2016, we entered into a license and collaboration agreement with Regeneron. The agreement includes a product component to research, develop and commercialize CRISPR/Cas-based therapeutic products primarily focused on genome editing in the liver as well as a technology collaboration component, pursuant to which we and Regeneron will engage in research and development activities aimed at discovering and developing novel technologies and improvements to CRISPR/Cas-based technology to enhance our genome editing platform. Under this agreement, we may access the Regeneron Genetics Center and proprietary mouse models to be provided by Regeneron for a limited number of our liver programs.

Agreement Structure

Under the terms of our collaboration, we and Regeneron have agreed to a target selection process, whereby Regeneron may obtain exclusive rights for up to 10 targets to be chosen by Regeneron during the collaboration term, subject to various adjustments and limitations set forth in the agreement. Of these 10 total targets, Regeneron may select up to five non-liver targets, while the remaining targets must be focused in the liver.

At the inception of the agreement, Regeneron selected the first of its 10 targets, which will be subject to a co-development and co-commercialization arrangement between us and Regeneron. We retain the exclusive right to solely develop products for the treatment of certain indications, including the genetic diseases primary hyperoxaluria ("PH-1") and alpha-1 antitrypsin deficiency ("AATD"). During the target selection process, we have the right to choose additional liver targets for our own development using commercially reasonable efforts. Certain targets that either we

or Regeneron select may be subject to further co-development and co-commercialization arrangements at our or Regeneron's option, as applicable, which either can exercise pursuant to defined conditions. In addition, subject to certain restrictions, Regeneron will be able to replace a limited number of targets with substitute targets upon the payment of a specified replacement fee, in which case exclusive rights to the replaced target revert to us. Regeneron's target selections are subject to certain additional restrictions, including that non-liver targets are not the subject of ongoing or planned research and development by us or are not the subject of a collaboration or pending collaboration with a third party.

Research activities under the collaboration will be governed by evaluation and research and development plans that will outline the parties' responsibilities under, anticipated timelines of and budgets for, the various programs. We will assist Regeneron with the preliminary evaluation of liver targets, and Regeneron will be responsible for preclinical research and the conduct of

clinical development, manufacturing and commercialization of products directed to each of its exclusive targets under the oversight of a joint steering committee. We may assist, as requested by Regeneron, with the later discovery and research of product candidates directed to any selected target. For each selected target, Regeneron is required to use commercially reasonable efforts to submit regulatory filings necessary to achieve initial IND acceptance for at least one product directed to each applicable target, and following IND acceptance for at least one product, to develop and commercialize such product.

In connection with this collaboration, Regeneron agreed to purchase $50.0 million of our common stock in a private placement concurrent with our initial public offering, and we received a nonrefundable upfront payment of $75.0 million. In addition, we are eligible to earn, on a per-licensed target basis, up to $25.0 million, $110.0 million and $185.0 million in development, regulatory and sales-based milestone payments, respectively. We are also eligible to earn royalties ranging from the high single digits to low teens, in each case, on a per-product basis, which royalties are potentially subject to various reductions and offsets and are further subject to our existing low- to mid-single-digit royalty obligations under a license agreement with Caribou Biosciences, Inc. (“Caribou”). In addition, Regeneron is obligated to fund 50.0 percent of certain research and development costs for the TTR program, the first target selected by Regeneron, which will be subject to a co-development and co-commercialization arrangement between us and Regeneron.

Collaboration Revenue

Through March 31, 2018, we recorded a $75.0 million upfront payment and $6.6 million for research and development services under the Regeneron agreement. Through March 31, 2018, we have recognized $30.6 million of collaboration revenue, including $5.1 million and $4.1 million during the three months ended March 31, 2018 and 2017, respectively, in the consolidated statements of operations related to this agreement. As of March 31, 2018 and December 31, 2017, we had deferred revenue of $51.0 million and $54.1 million, and accounts receivable of $6.5 million and $4.5 million, respectively, related to this agreement.

Results of Operations

The following table summarizes our results of operations for the three months ended March 31, 2018 and 2017:

| | Three Months Ended March 31, | | |
|---|---|---|---|
| | 2018 | 2017 | Increase / (decrease) |
| | (In thousands) | | |
| Collaboration revenue | $7,469 | $6,215 | $ 1,254 |
| Operating expenses: | | | |
| Research and development | 22,493 | 13,431 | 9,062 |
| General and administrative | 7,406 | 5,732 | 1,674 |
| Total operating expenses | 29,899 | 19,163 | 10,736 |
| Operating loss | (22,430) | (12,948) | (9,482) |
| Interest income | 1,074 | 317 | 757 |
| Net loss | $(21,356) | $(12,631) | $ (8,725) |

Collaboration Revenue

Collaboration revenue increased $1.3 million to $7.5 million during the three months ended March 31, 2018, as compared to $6.2 million during the three months ended March 31, 2017. The increase in collaboration revenue during the quarter ended March 31, 2018 is primarily related to the recognition of amounts under the Regeneron collaboration. The specific Regeneron related increase is driven by increased research and development services related to our TTR program, increasing to $2.0 million during the three months ended March 31, 2018 as compared to $0.9 million during the three months ended March 31, 2017.

Our revenue consists of collaboration revenue, including amounts recognized related to upfront technology access payments for licenses, technology access fees, research funding and milestone payments earned under our collaboration and license agreements with Novartis and Regeneron.

Research and Development

Research and development expenses increased $9.1 million to $22.5 million during the three months ended March 31, 2018, as compared to $13.4 million during the three months ended March 31, 2017. This increase is primarily related to an increase in research and development expenses of $5.3 million related to laboratory supplies, research materials and services for the further advancement of our early-stage research programs; and an increase in personnel-related costs of $3.7 million, which includes equity-based compensation expense, driven by our growth to 151 research and development employees as of March 31, 2018 from 88 research and development employees as of March 31, 2017.

Research and development expenses consist of expenses incurred in performing research and development activities, including compensation and benefits, which includes equity-based compensation, for full-time research and development employees, facility-related expenses, overhead expenses, lab supplies and contract research services.

Through 2018, we expect research and development expenses to increase as we continue to grow our research and development team and advance our research plans.

General and Administrative

General and administrative expenses increased $1.7 million to $7.4 million during the three months ended March 31, 2018, compared to $5.7 million during the three months ended March 31, 2017. This increase was primarily related to an increase of $1.6 million in personnel-related costs, which includes equity-based compensation expense, as we grew to 46 general and administrative employees as of March 31, 2018 from 31 general and administrative employees as of March 31, 2017.

General and administrative expenses consist primarily of salaries and benefits, including equity-based compensation, for our executive, finance, legal, business development and support functions. Other general and administrative expenses include allocated facility-related costs not otherwise included in research and development expenses, travel expenses and professional fees for auditing, tax and legal services, including intellectual property-related legal services, and other consulting fees and expenses.

Through 2018, we expect general and administrative expenses to increase as we continue to support the research and development team and advance our research plans.

Interest Income

Interest income increased by $0.8 million to $1.1 million during the three months ended March 31, 2018 as compared to $0.3 million during the three months ended March 31, 2017. This increase was caused by an increase in our average cash balance compared to the same period in the prior year.

Interest income is income earned on our cash equivalents. The increase in interest income is due to the increase in interest-bearing money market accounts, commercial paper and U.S. treasury securities, as compared to the same

period in the prior year.

Liquidity and Capital Resources

Since our inception through March 31, 2018, we have raised an aggregate of $508.6 million to fund our operations, of which $112.1 million was through our collaboration agreements, $170.5 million was from our initial public offering and concurrent private placements, $141.0 million was from a secondary offering and $85.0 million was from the sale of convertible preferred stock. As of March 31, 2018, we had $327.8 million in cash and cash equivalents.

In addition, we are entitled to receive technology access fees and research payments under our collaboration with Novartis and are also eligible to earn a significant amount of milestone payments and royalties, in each case, on a per-product basis under our collaboration with Novartis and on a per-target basis under our collaboration with Regeneron. Our ability to earn these milestones and the timing of achieving these milestones is dependent upon the outcome of our research and development activities and is uncertain at this time. Our rights to payments under our collaboration agreements are our only committed external source of funds.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, research and development services, compensation and related expenses, laboratory and related supplies, legal and other regulatory expenses, patent prosecution filing and maintenance costs for our licensed intellectual property and general overhead costs. During 2018, we expect our expenses to increase compared to prior periods in connection with our ongoing activities, particularly as we continue research and development and preclinical activities.

Because our research programs are still in preclinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of any future product candidates or whether, or when, we may achieve profitability. Until such time as we can generate substantial product revenues, if ever, we expect to finance our ongoing cash needs through equity financings and collaboration arrangements. We are entitled to technology access fees and research payments under our collaboration with Novartis. Additionally, we are eligible to earn milestone payments and royalties, in each case, on a per-product basis under our collaboration with Novartis and on a per-target basis under our collaboration with Regeneron. Except for these sources of funding, we will not have any committed external source of liquidity. To the extent that we raise additional capital through the future sale of equity, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Outlook

Based on our research and development plans and our expectations related to the progress of our programs, we expect that our cash and cash equivalents as of March 31, 2018, as well as technology access and research funding from Novartis and Regeneron, will enable us to fund our ongoing operating expenses and capital expenditures through mid-2020, excluding any potential milestone payments or extension fees that could be earned and distributed under the collaboration agreements with Novartis and Regeneron or any strategic use of capital not currently in the base case planning assumptions. We have based this estimate on current assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect.

Our ability to generate revenue and achieve profitability depends significantly on our success in many areas, including: developing our delivery technologies and our CRISPR/Cas9 technology platform; selecting appropriate product candidates to develop; completing research and preclinical and clinical development of selected product candidates; obtaining regulatory approvals and marketing authorizations for product candidates for which we complete clinical trials; developing a sustainable and scalable manufacturing process for product candidates; launching and commercializing product candidates for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor; obtaining market acceptance of our product candidates; addressing any competing technological and market developments; negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter; maintaining good relationships with our collaborators and licensors; maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and attracting, hiring, and retaining qualified personnel.

Cash Flows

The following is a summary of cash flows for the three months ended March 31, 2018 and 2017:

| | Three Months Ended March 31, | |
|---|---|---|
| | 2018 | 2017 |
| | (In millions) | |
| Net cash used in operating activities | $(17.8) | $(11.4) |
| Net cash used in investing activities | (1.9) | (4.2) |
| Net cash provided by financing activities | 6.7 | — |

Net cash used in operating activities

Net cash used in operating activities of $17.8 million during the three months ended March 31, 2018 primarily reflects increased spend in our research and development and general and administrative activities, offset in part by the receipt of $6.0 million from Novartis. Net cash used in operating activities of $11.4 million during the three months ended March 31, 2017 primarily reflects spend in our research and development and general and administrative activities, offset in part by the receipt of $6.0 million from Novartis.

Net cash used in investing activities

Net cash used in investing activities during the three months ended March 31, 2018 and 2017 relate to purchases of property and equipment as we grow our operations and build out our office and laboratory facilities.

Net cash provided by financing activities

Net cash provided by financing activities during the three months ended March 31, 2018 is made up of $6.7 million in cash received from the exercise of stock options.

Critical Accounting Policies

Our critical accounting policies require the most significant judgments and estimates in the preparation of our consolidated financial statements. Management has determined that our most critical accounting policies are those relating to revenue recognition and equity-based compensation. As discussed in Note 2 to our consolidated financial statements, we adopted Accounting Standards Update No. 2014-09, Revenue from Contracts with Customers (Topic 606) (“ASU 2014-09”) effective January 1, 2018. There have been no other significant changes to our critical accounting policies from those which were discussed in our Annual Report on Form 10-K for the year ended December 31, 2017.

Recent Accounting Pronouncements

Please read Note 2 to our consolidated financial statements included in Part I, Item 1, “Notes to Consolidated Financial Statements,” of this quarterly report on Form 10-Q for a description of recent accounting pronouncements applicable to our business.

Contractual Obligations

There were no material changes to our contractual obligations during the three months ended March 31, 2018. For a complete discussion of our contractual obligations, please refer to our Management’s Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the year ended December 31, 2017.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements as defined under the rules and regulations of the Securities and Exchange Commission.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of March 31, 2018, we had cash equivalents of $314.0 million consisting of interest-bearing money market accounts, commercial paper and U.S. treasury securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term maturities of our cash equivalents and the low risk profile of these investments, we believe that we do not have any material exposure to changes in the fair value of our investment portfolio as a result of changes in interest rates. Declines in interest rates, however, would reduce future investment income.

We do not have any foreign currency or other derivative financial instruments, and we do not believe that inflation had a material effect on our results of operations during the three months ended March 31, 2018. Inflation generally affects us by increasing our cost of labor and clinical trial costs.

Item 4. Controls and Procedures

Disclosure Controls and Procedures

The Company has established disclosure controls and procedures designed to ensure that information required to be disclosed in the reports that the Company files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer (our "Chief Executive Officer") and principal financial and accounting officer (our "Chief Financial Officer"), to allow timely decisions regarding required disclosure.

Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Quarterly Report on Form 10-Q. Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of March 31, 2018.

Changes in Internal Control over Financial Reporting

No change in the Company's internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended March 31, 2018 that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

PART II - OTHER INFORMATION

Item 1. Legal Proceedings

In the ordinary course of business, we are from time to time involved in lawsuits, claims, investigations, proceedings, and threats of litigation related to intellectual property, commercial arrangements and other matters. “Item 3. Legal Proceedings” of our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 includes discussions of our current legal proceedings. There have been no material changes to those disclosures as of the date of this filing.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Quarterly Report on Form 10-Q, our Annual Report on Form 10-K for the year ended December 31, 2017 and in other documents that we file with the SEC, in evaluating the Company and our business. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks facing the Company. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations.

Risks Related to Our Business, Technology and Industry

CRISPR/Cas9 genome editing technology is not yet clinically validated for human therapeutic use. The approaches we are taking to discover and develop novel therapeutics using CRISPR/Cas9 systems are unproven and may never lead to marketable products. If we are unable to develop viable product candidates, achieve regulatory approval for any such product candidate or market and sell any product candidates, we may never achieve profitability.

We are focused on developing curative medicines utilizing the CRISPR/Cas9 genome editing technology. Although there have been significant advances in the fields of gene therapy, which typically involves introducing a copy of a gene into a patient’s cell, and genome editing in recent years, CRISPR-based genome editing technologies are relatively new, and their therapeutic utility is largely unproven. The CRISPR/Cas9 technologies that we intend to develop have not yet been clinically tested by us, and we are not aware of any clinical trials for safety or efficacy having been completed by third parties involving these technologies. The scientific evidence to support the feasibility of developing products based on these technologies is both preliminary and limited. Successful development of products by us will require solving a number of issues, including developing or obtaining technologies to safely deliver a therapeutic agent into target cells within the human body or modify human cells while outside of the body such that the modified cells can have a therapeutic effect when delivered to the patient, optimizing the efficacy and specificity of such products, and ensuring the therapeutic selectivity and efficacy of such products. There can be no assurance we will be successful in solving any or all of these issues.

We have principally concentrated our research efforts to date on bringing CRISPR/Cas9-based therapeutics to the clinic for various initial indications, and our future success is highly dependent on the successful development of CRISPR-based genome editing technologies, cellular delivery methods and therapeutic applications for these indications. These indications are the principal focus of our initial development efforts, and we may decide to alter or abandon these programs as new data become available and we gain experience in developing CRISPR/Cas9-based

therapeutics. We cannot be sure that our CRISPR/Cas9 technologies will yield satisfactory products that are safe and effective, scalable or profitable in our selected indications or any other indication we pursue.

Public perception and related media coverage of potential therapy-related efficacy or safety issues, including adoption of new therapeutics or novel approaches to treatment, as well as ethical concerns related specifically to genome editing and CRISPR/Cas9, may adversely influence the willingness of subjects to participate in clinical trials, or if any therapeutic is approved, of physicians and patients to accept these novel and personalized treatments. Physicians, health care providers and third-party payors often are slow to adopt new products, technologies and treatment practices, particularly those that may also require additional upfront costs and training. Physicians may not be willing to undergo training to adopt these novel and personalized therapies, may decide the particular therapy is too complex or potentially risky to adopt without appropriate training, and may choose not to administer the therapy. Further, due to health conditions, genetic profile or other reasons, certain patients may not be candidates for the therapies. In addition, responses by the U.S., state or foreign governments to

negative public perception, ethical concerns or financial considerations may result in new legislation, regulations, or medical standards, that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval or otherwise achieve profitability. Based on these and other factors, health care providers and payors may decide that the benefits of these new therapies do not or will not outweigh their costs.

Our ability to generate product revenue is dependent on the success of our application of CRISPR/Cas9 technology for human therapeutic use, which is at an early stage of development and will require significant additional discovery efforts, preclinical testing and clinical studies, as well as applicable regulatory guidance for preclinical testing and clinical studies from the Food and Drug Administration ("FDA") and other regulatory authorities, before we can seek regulatory approval and begin commercial sales of any potential product candidates.

Our ability to generate product revenue is highly dependent on our ability to obtain regulatory approval of and successfully commercialize one or more of our product candidates. Any product candidates we discover will require preclinical, clinical and regulatory review and approval in each jurisdiction in which we intend to market the products, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. Before obtaining marketing approval from regulatory authorities for the sale of a product candidate, we must conduct extensive clinical trials to demonstrate the safety, purity and potency, as well as the effectiveness of the product candidates in humans. We cannot be certain that any of our product candidates will be successful in clinical trials and, even if successful, they may not receive regulatory approval.

Our approach to developing therapies for genetic and viral-based diseases centers on using the CRISPR/Cas9 technology to introduce or remove genetic information in vivo to treat various disorders, or to modify human cells ex vivo to create therapeutic cells that can be introduced into the human body to address the underlying disease. Because these are new therapeutic approaches, discovering, developing and commercializing our product candidates subject us to a number of challenges, including:

- obtaining regulatory approval from the FDA and other regulatory authorities that have very limited or no experience with the clinical development of CRISPR/Cas9 therapeutics;
- seeking and obtaining regulatory approval from the FDA and other regulatory authorities in light of no formal guidance regarding potential regulatory pathways for this category of in vivo therapeutics, including preclinical and clinical requirements for approval of an IND;
- educating medical personnel regarding the potential benefits and side effect profile of each of our product candidates;
- developing processes for the safe administration of these products, including long-term follow-up for all patients who receive treatment with any of our product candidates;
- sourcing clinical and, if approved, commercial supplies for the materials used to manufacture and process our product candidates;
- developing a manufacturing process and distribution network with a cost of goods that allows for an attractive return on investment; and
- establishing sales and marketing capabilities in anticipation of and after obtaining any regulatory approval to gain market acceptance.

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

- regulatory guidance regarding the requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. To date, only a limited number of products that involve the in vivo genetic modification of patient cells have been approved globally;
- improper insertion of a gene sequence into a patient's chromosome could lead to cancer, other aberrantly functioning cells or other diseases, including death;

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- 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 such an observation period for our product candidates; and
- clinical trials using therapies that genetically modify cells conducted at institutions that receive funding for recombinant DNA research from the NIH, may be subject to review by the RAC. Although the FDA decides whether individual protocols may proceed, the RAC review process can impede the initiation of a clinical trial, even if the FDA has reviewed the study and it has become effective under an IND.

Further, because our ex vivo product candidates involve gene editing human cells and then manufacturing and delivering modified cells to patients, we are subject to many of the challenges and risks that cell therapies face, including:

- clinical trials using genetically modified cells conducted at institutions that receive funding for recombinant DNA research from the National Institutes of Health ("NIH"), may be subject to review by the Recombinant DNA Advisory Committee ("RAC"). Although the FDA decides whether individual protocols may proceed, the RAC review process can impede the initiation of a clinical trial, even if the FDA has reviewed the study and it has become effective under an IND; and
- clinical trials using engineered cell therapies require unique products to be created for each patient and such individualistic manufacturing may be both inefficient and cost-prohibitive.

To date, although human clinical trials for other in vivo genome editing-based therapeutics have been authorized by the FDA, neither we nor any other company has received regulatory approval in the U.S. or EU to commence human clinical trials utilizing in vivo CRISPR/Cas9-based therapeutics or to market in vivo therapeutics utilizing any genome editing technology, including CRISPR/Cas9. There is no certainty that the FDA or European Medicines Agency ("EMA") will apply to CRISPR/Cas9 product candidates the same regulatory pathway and requirements it is applying to other in vivo genome editing-based therapeutics; and the FDA and other regulatory authorities have not yet provided written guidance regarding preclinical or clinical studies or regulatory approval pathways specific for in vivo genome editing-based therapeutics. In addition, if any product candidates encounter safety or efficacy problems, developmental delays, regulatory issues or other problems, our development plans and business could be significantly harmed. Further, competitors that are developing in vivo products with similar technology may experience problems with their product candidates or programs that could in turn cause us to identify problems with our product candidates and programs that would potentially harm our business.

Further, significant uncertainty exists regarding the future scope and effect of the FDA's regulatory framework, in particular relating to the review and approval of human therapeutic products because the current U.S. administration and federal legislators have publicly declared their intention to significantly modify the current legal framework governing the FDA. Any such changes to the FDA requirements could impact our ability to obtain approval for our products or sell them profitably. In addition, in the EU, the decision of the United Kingdom to withdraw from the EU has required the EMA to relocate to the Netherlands, and recruit and retain new personnel to review and approve our submissions for regulatory approval in Europe. EMA's relocation could result in delays and other changes that may impact the timing and our ability to obtain approval for our products. Also, upon exiting the EU, the United Kingdom may enact legislation related to the approval and oversight of human therapeutics in that nation. Until any such legislation is enacted, we will be uncertain as to its effects on our business, including our ability to seek and obtain approval for our products in the United Kingdom.

In addition, during fiscal year 2017, non-commercial entities have commenced human trials involving in vivo CRISPR/Cas9-based therapeutics in China. Neither these entities nor the Chinese regulatory agencies have shared publicly any information on the regulatory process for clinical trial approval including specific protocol requirements. Any specific requirement from the Chinese regulatory agencies may impact our ability to submit or obtain approval for our products in China. Further, if these human trials are unsuccessful, or if they result in significant adverse events, including deaths, there could be a significant impact to the evaluation of our product candidates globally, as well as an increase in negative public opinion.

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Even if we obtain regulatory approval of any product candidates, such candidates may not gain market acceptance among physicians, patients, hospitals, third-party payors and others in the medical community.

The use of the CRISPR/Cas9 system as a framework for developing gene editing-based therapies is a recent development and may not become broadly accepted by physicians, patients, hospitals, third-party payors and others in the medical community. A variety of factors will influence whether our product candidates are accepted in the market, including, for example:

- the clinical indications for which our product candidates are approved;
- the potential and perceived advantages of our product candidates over alternative treatments;
- the incidence and severity of any side effects, including off-target editing or immunogenicity;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA or other regulatory authorities;
- the timing of market introduction of our product candidates;
- availability or existence of competitive products;
- the cost of treatment in relation to alternative treatments;
- the amount of upfront costs or training required for health care providers to administer our product candidates;
- the availability of adequate coverage, reimbursement and pricing by third-party payors and government authorities;
    - patients' ability to access physicians and medical centers capable of delivering any therapies that we develop;
- the willingness of patients to pay out of pocket in the absence of coverage and reimbursement by third-party payors and government authorities;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies;
- any restrictions on the use of our product candidates together with other medications;
- interactions of our product candidates with other medicines patients are taking;
- potential adverse events for any products developed, or negative interactions with regulatory agencies, by us or others in the gene therapy and gene editing fields; and
- the effectiveness of our sales and marketing efforts and distribution support.

Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete. In addition, adverse publicity due to the ethical and social controversies surrounding the therapeutic in vivo use of CRISPR/Cas9, gene edited modified cells, or other therapeutics mediums, such as viral vectors that we may use in our clinical trials may limit market acceptance of our product candidates. If our product candidates are approved but fail to achieve market acceptance among physicians, patients, hospitals, third-party payors or others in the medical community, we will not be able to generate significant revenue.

Negative public opinion and increased regulatory scrutiny of in vivo CRISPR/Cas9 use, gene editing or gene therapy generally may damage public perception of the safety of any product candidates that we develop and adversely affect our ability to conduct our business or obtain regulatory approvals for such product candidates.

Gene therapy in general, and gene editing in particular, remain novel technologies, with only a limited number of gene therapy products approved to date in the U.S. and EU. Public perception may be influenced by claims that gene therapy or gene editing, including the use of CRISPR/Cas9, is unsafe or unethical, and gene therapy or gene editing may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians who specialize in the treatment of diseases targeted by our product candidates prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments with which they are more familiar and for which greater clinical data may be available. In

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addition, responses by the U.S., state or foreign governments to negative public perception or ethical concerns may result in new legislation or regulations that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval or otherwise achieve profitability. More restrictive statutory regimes, government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, earlier gene therapy trials led to several well-publicized adverse events, including cases of leukemia and death, and the FDA has previously initiated a clinical hold on a CAR-T cell therapy clinical trial due to patient deaths, and the company developing the therapy ultimately decided to stop the program. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy or gene editing products or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidate.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, if approved, which could make it difficult for us to sell any product candidates or therapies profitably.

The success of our product candidates, if approved, depends on the availability of adequate coverage and reimbursement from third-party payors, including government agencies. In addition, because our product candidates represent new approaches to the treatment of genetic-based diseases, we cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors are critical to new product acceptance.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

In the U.S., no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of our gene-modifying products. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. Because our product candidates may have a higher cost of goods than conventional therapies, and may require long-term follow up evaluations, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater. There is significant uncertainty

related to insurance coverage and reimbursement of newly approved products. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Moreover, increasing efforts by governmental and third-party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes.

We intend to seek approval to market our product candidates in both the U.S. and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. In some foreign countries, particularly those in the EU, the pricing of pharmaceutical products, including biologics, is subject to governmental control and other market regulations which could put pressure on the pricing and usage of our product candidates. In these countries, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for our product candidates and may be affected by existing and future health care reform measures.

Research and development of biopharmaceutical products is inherently risky. We may not be successful in our efforts to use and enhance our gene editing technology to create a pipeline of product candidates, obtain regulatory approval and develop commercially successful products, or we may expend our limited resources on programs that do not yield a successful product candidate and fail to capitalize on potential product candidates or diseases that may be more profitable or for which there is a greater likelihood of success. If we fail to develop product candidates, our commercial opportunity, if any, will be limited.

We have not currently selected any particular product candidates for clinical development. We are at an early stage of development and our technology and approach has not yet led, and may never lead, to any product candidate appropriate for clinical development or any approved or commercially successful products. Even if we are successful in building our pipeline of product candidates, completing clinical development, obtaining regulatory approvals and commercializing product candidates will require substantial additional funding and are prone to the risks of failure inherent in therapeutic product development. Investment in biopharmaceutical product development involves significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, or become commercially viable.

We cannot provide any assurance that we will be able to successfully advance any product candidates that we discover through the research process. Our research programs may initially show promise, yet fail to yield product candidates for clinical development or commercialization for many reasons, including the following:

- our technology and approach may not be successful in identifying product candidates for clinical development and commercialization;
- we may not be able or willing to assemble sufficient resources to acquire or discover product candidates for clinical development and commercialization;
- animal or other non-human models for the targeted disease may not be appropriate or available to conduct preclinical testing;
- testing in preclinical models may not be predictive of human clinical testing results because species have distinct genomic sequences that may require the use of species-specific guides and reagents;
- our product candidates may not succeed in preclinical or clinical testing;
- our planned risk mitigation strategy for selecting our initial indications may fail or we may not be able to efficiently apply learnings from our initial development programs to future development programs;
- we may be unable to optimize the therapeutic efficiency, specificity, or selectivity of our future product candidates;

- our therapeutic delivery systems may fail so that even a product candidate with therapeutic activity might not demonstrate a clinically meaningful therapeutic effect;

- a product candidate may not demonstrate in patients the biological, chemical and pharmacological properties identified in laboratory and preclinical studies, or they may interact with human biological systems in unforeseen, ineffective or even harmful ways;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- the therapeutic effect of a product candidate may not be permanent and may diminish over time;
- a single treatment course may not be sufficient for a cure or therapeutic benefit, and it may take several treatment courses for the product to be effective;
- a well-defined and achievable pathway to regulatory approval may never materialize for a specific product candidate;
- competitors may develop alternatives that render our product candidates obsolete, redundant or less attractive;
- product candidates we develop may be covered by third-party or other exclusive rights or may not receive desired regulatory exclusivity, and we may be unable to maintain, expand or protect our intellectual property rights;
- the market for a product candidate may change during our program so that the continued development of that product candidate is no longer reasonable;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- we may be unable to successfully maintain existing collaborations or licensing arrangements or enter into new ones throughout the development process as appropriate; and
- a product candidate may not be accepted as safe and effective by physicians, patients, hospitals, third-party payors and others in the medical community.

If any of these events occur, we may be forced to abandon our development efforts for a product candidate, program or programs, or we may not be able to identify, discover, develop or commercialize product candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Because we have limited financial and managerial resources, we are initially focused on specific research programs. As a result, we may fail to capitalize on other viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights. For additional information regarding the factors that will affect our ability to achieve revenue from product sales, see the risk factor entitled “We have never generated any revenue from product sales and our ability to generate revenue from product sales and become profitable depends significantly on our success in a number of factors.”

If we do not successfully develop and commercialize product candidates based upon our approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price. Further, our current focus on CRISPR/Cas9 technology for developing products as opposed to multiple, more proven technologies for product development increases the risk associated with our business. If we are not successful in developing a product candidate using CRISPR/Cas9 technology, we may not be able to successfully implement an alternative product development strategy.

Results, including positive results, from our initial pre-clinical studies are not necessarily predictive of our other ongoing and future pre-clinical and clinical studies, and they do not guarantee or indicate the likelihood of approval of any potential product candidate by the FDA, EMA or any other regulatory agency. If we cannot replicate the positive results from any of our pre-clinical or clinical studies, we may be unable to successfully develop, obtain regulatory approval for and commercialize any potential product candidate.

There is a high failure rate for product candidates progressing through pre-clinical and clinical studies. Even if we are able to successfully complete our ongoing and future pre-clinical studies for any potential product candidate, we may not be able to replicate any positive results from these or any other studies in any of our future pre-clinical and clinical

trials, and they do not guarantee approval of any potential product candidate by the FDA, EMA or any other necessary regulatory authorities in a

timely manner or at all. Companies in the pharmaceutical and biotechnology industries have commonly suffered significant setbacks in clinical studies 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 findings made before, during and after clinical studies were underway, or observations regarding the lack of safety or efficacy made in clinical studies, which could include new or previously unreported adverse events. In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in the relevant laws, regulations or regulatory policy during the period of product development.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in such studies nonetheless failed to obtain FDA, EMA or other necessary regulatory agency approval. If we fail to obtain results in our on-going, planned and future pre-clinical and clinical studies sufficient to meet the requirements of the relevant regulatory agencies, the development timeline and regulatory approval and commercialization prospects for any potential product candidate, and, correspondingly, our business and financial prospects, would be materially adversely affected.

The reported results of our NHP studies are based on top-line interim data and may ultimately differ from actual results once additional data are received and fully evaluated.

The reported results of the NHP studies that we have publicly disclosed, and that are discussed herein and in documents we incorporated by reference, consist of top-line interim data. Top-line interim data are based on a preliminary analysis of currently-available data from an ongoing series of studies, and therefore the reported results, findings and conclusions related to these data are subject to change following a comprehensive review of the more extensive data that we expect to receive related to the studies. Our reported results and related top-line interim data are based on assumptions, estimations, calculations and information currently available to us, and we have not received or had an opportunity to fully evaluate all of the data related to the studies. As a result, the top-line interim data results that we have reported may differ from future results, or different conclusions or considerations may qualify such results, once the current data or additional data have been received and fully evaluated. In addition, third parties, including regulatory agencies, may not accept or agree with our assumptions, estimations, calculations or analyses, or may interpret or weigh the importance of data differently, which could impact the value of our technology, the approvability or commercialization of product candidates and our business in general. If the top-line interim data that we have reported related to NHP differ from actual results or is perceived as insufficient or faulty, our ability to obtain approval for, and commercialize, our products may be harmed, which could harm our business, financial condition, operating results or prospects.

Clinical development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.

All of our lead programs are still in the discovery or preclinical stage, and their risk of failure is high. It is impossible to predict when or if any of our programs will prove effective and safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of any of our future product candidates in humans. Preclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. We may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, and a clinical trial can fail at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to

obtain marketing approval of their products.

Successful completion of clinical trials is a prerequisite to submitting a New Drug Application ("NDA") or Biologics License Application ("BLA") to the FDA, a Marketing Authorization Application to the EMA and similar filings to comparable foreign regulatory authorities, for each product candidate and, consequently, the ultimate approval and commercial marketing of any product candidates. We do not know whether any of our clinical trials will begin or be completed on schedule, if at all.

We may experience delays in completing our preclinical studies and initiating or completing clinical trials. We also may experience numerous unforeseen events during, or as a result of, any future clinical trials that we could conduct, which could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators, institutional review boards ("IRB"s) or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations ("CRO"s), the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of any product candidates may fail to show safety or efficacy, produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- the number of patients required for clinical trials of any product candidates may be larger than we anticipate, enrollment in these clinical trials may be lower than required by the regulatory agencies or slower than we anticipate, or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
    - we may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of preclinical studies and clinical trials of any product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, IRBs or ethics committees to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other gene therapies or gene editing-based therapies that raise safety or efficacy concerns about our product candidates; and
- the FDA or other regulatory authorities may require us to submit additional data, such as long-term toxicology studies, or impose other requirements before permitting us to initiate or rely on a clinical trial.

We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, the Data Safety Monitoring Board ("DSMB") for such trial or FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by FDA or other regulatory authorities resulting in the imposition of a clinical hold, manufacturing or quality control issues, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials.

Our product development costs will increase if we experience delays in clinical testing or marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods

during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations. Any delays in our preclinical or future clinical development programs may harm our business, financial condition and prospects significantly.

Inconclusive results, lack of efficacy, adverse events or additional safety concerns in clinical trials that we or others conduct may impede the regulatory approval process or overall market acceptance of our future product candidates.

Therapeutic applications of gene editing technologies, and CRISPR/Cas9 in particular, for both in vivo products and in engineered cell therapies, are unproven and must undergo rigorous clinical trials and regulatory review before receiving marketing authorization. If the results of our clinical studies or those of any other third parties, including with respect to gene editing technology or engineered cell therapies, are inconclusive, fail to show efficacy or if such clinical trials give rise to safety concerns or adverse events, we may:

- be delayed in obtaining marketing approval for our future product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to the addition of labeling statements, such as warnings or contraindications, or other types of regulatory restrictions or scrutiny;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical studies to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities modify or withdraw their legal requirements or written guidance, if any, regarding the applicable regulatory approval pathway or any approval of the product in question, or impose restrictions on its distribution in the form of a modified REMS;
- be sued; or
- experience damage to our reputation.

Additionally, our future product candidates could potentially cause other adverse events that have not yet been predicted and the potentially permanent nature of gene editing effects, including CRISPR/Cas9's effects, on genes or novel cell therapies in the organs of the human body may make these adverse events irreversible. The inclusion of critically ill patients in our clinical studies or those of our competitors may result in deaths or other adverse medical events, including those due to other therapies or medications that such patients may be using. Any of these events could prevent us from achieving or maintaining regulatory approval or market acceptance of our future product candidates and impair our ability to achieve profitability.

We have never generated any revenue from product sales and our ability to generate revenue from product sales and become profitable depends significantly on our success in a number of areas.

We have no products approved for commercial sale, have not generated any revenue from product sales, and do not anticipate generating any revenue from product sales until sometime after we have received regulatory approval for the commercial sale of a product candidate that we discover. Our ability to generate revenue and achieve and retain profitability depends significantly on our success in many areas, including:

- selecting commercially viable product candidates and effective delivery methods;
- completing research, preclinical and clinical development of product candidates;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we complete clinical trials;
- developing a sustainable and scalable manufacturing process for product candidates, including establishing and maintaining commercially viable supply relationships with third parties and potentially establishing our own manufacturing capabilities and infrastructure;
- launching and commercializing product candidates for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor;
- accurately assessing the size and addressability of potential patient populations;
- obtaining market acceptance of our product candidates as viable treatment options;

- addressing any competing technological and market developments;

- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter or which may be necessary for us to develop, manufacture or commercialize our product candidates;
- maintaining good relationships with our collaborators and licensors;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- avoiding infringement of or obtaining licenses to any valid intellectual property owned or controlled by third parties; and
- attracting, hiring and retaining qualified personnel.

Even if one or more product candidates that we discover and develop are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate and the timing of such costs may be out of our control. Our expenses could increase beyond expectations if we are required by the FDA or other regulatory agencies, domestic or foreign, to change our manufacturing processes or assays, or to perform clinical, nonclinical or other types of additional studies. If we are successful in obtaining regulatory approvals to market one or more product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price and whether we own the commercial rights for that territory. If the number of our addressable disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. If we are not able to generate revenue from the sale of any approved products, we may never become profitable.

We face significant competition in an environment of rapid technological change. The possibility that our competitors may achieve regulatory approval before we do or develop therapies that are more advanced or effective than ours may harm our business and financial condition or our ability to successfully market or commercialize our product candidates.

The biotechnology and pharmaceutical industries, including the gene editing field and cell therapies, 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.

Competitors in our efforts to provide genetic therapies to patients can be grouped into at least three sets based on their product discovery platforms:

- genome editing companies focused on CRISPR/Cas9 including: Casebia Therapeutics, LLC, CRISPR Therapeutics, Inc., Editas Medicine, Inc., ToolGen, Inc. and Tracr Hematology Limited;
- other genome editing companies including: bluebird bio, Inc., Cellectis S.A., Homology Medicines, Inc., Poseida, Inc., Precision BioSciences, Inc. and Sangamo Therapeutics, Inc.; and
- genome therapy companies developing in vivo or ex vivo therapies, such as cell therapies, including: bluebird bio, Inc., Cellectis S.A., Celgene Corporation (which acquired Juno Therapeutics, Inc.), Gilead Sciences, Inc. (which acquired Kite Pharma, Inc.), Novartis A.G. and Spark Therapeutics, Inc.

Our competitors will also include companies that are or will be developing other genome editing methods as well as small molecules, biologics, in vivo gene therapies, ex vivo cell therapies and nucleic acid-based therapies for the same indications that we are targeting with our CRISPR/Cas9-based therapeutics.

Any advances in gene therapy, cell therapies or gene editing technology made by a competitor may be used to develop therapies that could compete against any of our product candidates. Many of these competitors have substantially greater research and development capabilities and financial, scientific, technical, intellectual property, manufacturing, marketing, distribution and other resources than we do, and we may not be able to successfully compete with them.

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To become and remain profitable, we must discover, 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 product candidates, obtaining marketing approval for product candidates, manufacturing, marketing and selling products that are approved and satisfying any post-marketing requirements. Even if we are successful in selecting and developing any product candidates, in order to compete successfully we may need to be first-to-market or demonstrate that our CRISPR/Cas9-based products are superior to therapies based on the same or different treatment methods. If we are not first-to-market or are unable to demonstrate such superiority, any products for which we are able to obtain approval may not be successful. Furthermore, in certain jurisdictions, if a competitor has orphan drug status for a product and if our product candidate is determined to be contained within the scope of a competitor's orphan drug exclusivity, then approval of our product for that indication or disease could potentially be blocked, for example, for up to seven years in the U.S. and 10 years in the EU.

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 the Company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

We have a very limited operating history, which may make it difficult to evaluate our current business and predict our future performance.

We are very early in our development efforts and all of our lead programs are still in the discovery stage. We were formed in May 2014, 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.

Each of our programs may require additional discovery research and then preclinical and 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 foreign regulatory agencies, including the 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 current business and predict our future performance. Our very 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 very early stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

We have incurred net losses in each period since our inception, anticipate that we will continue to incur net losses in the future and may never achieve profitability.

We are not profitable and have incurred losses in each period since our inception. Our net loss was $21.4 million for the three months ended March 31, 2018. As of March 31, 2018, we had an accumulated deficit of $137.0 million. We expect these losses to increase as we continue to incur significant research and development and other expenses related to our ongoing operations, seek regulatory approvals for our future product candidates, scale-up manufacturing capabilities, maintain, expand and protect our intellectual property portfolio and hire additional personnel to support the development of our product candidates and to enhance our operational, financial and information management

systems.

A critical aspect of our strategy is to invest significantly in our technology to improve the efficacy and safety of potential product candidates that we discover. Even if we succeed in discovering, developing and ultimately commercializing one or more of these product candidates, we will continue to incur losses for the foreseeable future relating to our substantial research and development expenditures to develop our technologies. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Further, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We may need to raise substantial additional funding to fund our operations. If we fail to obtain additional financing, we may be unable to complete the development and commercialization of any product candidates.

Our operations have required substantial amounts of cash since inception, and we expect to spend substantial amounts of our financial resources on our discovery programs going forward and future development efforts. If we are able to identify product candidates that are eventually approved, we will require significant additional amounts in order to launch and commercialize our product candidates. For the foreseeable future, we expect to continue to rely on additional financing to achieve our business objectives.

We will require additional capital for the further development and commercialization of any product candidates and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate or due to other unanticipated factors.

We cannot be certain that additional funding will be available on acceptable terms, or at all. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Our collaboration and license agreements may also be terminated if we are unable to meet the payment or other obligations under the agreements. We could be required to seek collaborators for product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Raising additional capital may cause dilution to our stockholders and restrict our operations.

We will need additional capital in the future to continue our planned operations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our ability to complete clinical trials or our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for any future product candidates 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 similar regulatory authorities outside the U.S. If patients are unwilling to participate in our clinical studies because of concerns about, or negative publicity from, adverse events in the gene editing field, the novel nature of the CRISPR/Cas9 gene editing technology, the irreversibility of the effects of CRISPR/Cas9 or for other reasons, including competitive clinical studies for similar patient populations, then the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical studies altogether. In addition, any patients who would otherwise be eligible for clinical trials that we may hold may instead enroll in clinical trials of product candidates of our competitors.

Patient enrollment is affected by other factors including:

- the size, location and nature of the patient population;
- the severity of the disease under investigation;
- the patient eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the design of the clinical trial;
- our payments for conducting clinical trials;

- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in clinical trials may result in increased development costs for any of our potential future product candidates, which would cause the value of the Company to decline and limit our ability to obtain additional financing. Furthermore, we expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and, while we expect to enter into agreements governing their committed activities, we will have limited influence over their actual performance.

We expect to expand our research, development and regulatory capabilities, and, as a result, we may encounter difficulties in hiring capable personnel and otherwise managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of technology research, product development and manufacturing, clinical and regulatory affairs and, if any product candidates are submitted for or receive marketing approval, sales, marketing and distribution. To manage our anticipated future growth, 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. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to recruit and train additional qualified personnel or to otherwise effectively manage the expansion of our operations. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business and development plans or disrupt our operations.

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, legal, financial and business development expertise of John M. Leonard, M.D., our President and Chief Executive Officer, Graeme Bell, our Executive Vice President, Chief Financial Officer, and José E. Rivera, our Executive Vice President, General Counsel, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment arrangements 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.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be important for our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products using our technology. Competition to hire from this limited pool is intense, and 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, universities and research institutions for similar personnel. The market for qualified personnel in the biotechnology space generally, and gene editing and gene therapy fields in particular, in and around the Cambridge, Massachusetts area is especially competitive. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. 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. Further, some of the qualified personnel that we hire and recruit are not U.S. citizens, and there is uncertainty with

regard to their future employment status due to the current U.S. administration's announced intention of modifying the legal framework for non-U.S. citizens to be employed in the U.S. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

If, in the future, we are unable to establish sales, marketing and distribution capabilities or enter into agreements with third parties to sell, market and distribute products based on our technologies, we may not be successful in commercializing our products if and when any products candidates or therapies are approved and we may not be able to generate any revenue.

We do not currently have a sales, marketing or distribution 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 they 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 candidates 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;
- the location of patients in need of our product candidates and the treating physicians who may prescribe the products; and
- unforeseen costs and expenses, as well as legal and regulatory requirements, associated with creating and operating a 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.

Our technological advancements and any potential for revenue may be derived in part from our collaborations with Novartis and Regeneron, and if either of these collaboration agreements were to be terminated, our business, financial condition, results of operations and prospects would be harmed.

In December 2014, we entered into a collaboration agreement with Novartis regarding the discovery of new CRISPR/Cas9-based therapies principally using CAR-T cells and HSCs. Under the Novartis collaboration agreement, we received a commitment to advance multiple programs. Pursuant to the Novartis agreement, we granted Novartis exclusive rights to further develop and commercialize products arising out of the CAR-T cell program during the research term. Regarding HSCs, we are jointly advancing multiple programs with Novartis and have agreed to a

process for assigning development and ownership rights, which may enable us to develop our own proprietary HSC pipeline.

In April 2016, we entered into a collaboration agreement with Regeneron that includes a product component to research, develop and commercialize CRISPR/Cas-based therapeutic products primarily focused on gene editing in the liver as well as a technology collaboration component, pursuant to which we and Regeneron will engage in research and development activities aimed at discovering and developing novel technologies and improvements to CRISPR/Cas technology to enhance our gene editing platform. Pursuant to the Regeneron collaboration agreement, we granted Regeneron exclusive rights to select up to 10

targets, subject to certain restrictions, while we retain the rights to solely develop our initial indications, other than ATTR, which will be subject to a co-development and co-commercialization arrangement with Regeneron, and have the right to choose additional liver targets for our own development during the collaboration term. Certain other of the development targets under the Regeneron agreement may also be subject to a co-development/co-commercialization arrangement with the other party at the other party's option.

Either Novartis or Regeneron may change its strategic focus or pursue alternative technologies in a manner that results in reduced, delayed or no revenue to us. Each of Novartis and Regeneron has a variety of marketed products and product candidates either by itself or under collaboration with other companies, including some of our competitors, and the respective corporate objectives of Novartis or Regeneron may not be consistent with our best interests. If either of our collaboration partners fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate from the development programs governed by the respective collaboration agreement in the applicable territories, or if either of our collaboration partners terminates our collaboration with it, our business, financial condition, results of operations and prospects could be harmed. In addition, any dispute or litigation proceedings we may have with either Novartis or Regeneron in the future could delay development programs, create uncertainty as to ownership of or access to intellectual property rights, distract management from other business activities and generate substantial expense.

Our existing and future collaborations will be important to our business. If we are unable to maintain any of these collaborations, or if these collaborations are not successful, our business could be adversely affected.

We have limited capabilities for product discovery and development and do not yet have any capability for sales, marketing or distribution. Accordingly, we have entered, and plan to enter, into collaborations with other companies, including our therapeutic-focused collaboration agreements with Novartis and Regeneron, that we believe can provide such capabilities. These therapeutic-focused collaborations provide us with important technologies and funding for our programs and technology, and we expect to receive additional technologies and funding under these and other collaborations in the future. Our existing therapeutic collaborations, and any future collaborations we enter into, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply;
- collaborators may not perform their obligations as expected;
- collaborators may dispute the amounts of payments owed;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs or license arrangements based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could develop independently or with third parties products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
    - product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the development or commercialization of our product candidates;
- collaborators may fail to comply with applicable legal and regulatory requirements regarding the development, manufacture, sale, distribution or marketing of a product candidate or product;
- collaborators with sale, marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the sale, marketing and distribution of such product or

products;

- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation, payment obligations or the preferred course of discovery, development, sales or marketing, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional and burdensome responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend their or our relevant intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation and liability;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- if a collaborator of ours is involved in a business combination or cessation, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us; and
- collaborations may be terminated by the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our therapeutic collaborations do not result in the successful discovery, development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development and commercialization of our technology and product candidates could be delayed and we may need additional resources to develop product candidates and our technology. All of the risks relating to product discovery, development, regulatory approval and commercialization described in this report also apply to the activities of our therapeutic collaborators.

Additionally, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

For some of our programs, we may in the future determine to collaborate with pharmaceutical and biotechnology companies for discovery, development and potential commercialization of therapeutic products. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for a collaboration 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. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail discovery efforts or the development of a product candidate, 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 fund and undertake discovery, development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary discovery, development and commercialization activities, we may not be able to further develop our product candidates, bring them to market or continue to develop our technology and our business may be materially and adversely affected.

Gene editing products and engineered cell therapies 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 in vivo and ex vivo product candidates, including engineered cell therapies, 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 unavailability or contamination; raw material cost, shortages or contamination; natural disasters; disruption in utility

services; human error; insufficient personnel; inability to meet legal or regulatory requirements; or disruptions in the operations of our suppliers.

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 a complex product such as ours generally cannot be fully characterized. As a result, assays of the finished product or relevant components 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 and litigation, insufficient inventory or production interruption. We may encounter problems achieving adequate quantities and quality of clinical grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA and other foreign 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 foreign 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, product recalls or production interruption. Lot failures, product recalls or production interruption 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 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.

We expect to rely in part 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 or fail to meet legal and regulatory requirements.

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and must eventually rely on outside vendors to manufacture supplies and process our 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, potent or effective.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA or other foreign regulatory agencies pursuant to inspections that will be conducted after we submit an application to the FDA or other foreign regulatory agencies. We will be dependent on our contract manufacturing partners for compliance with legal and regulatory requirements for manufacture, including current good manufacturing practice (“cGMP”), and in certain cases, current good tissue practice (“cGTP”), requirements 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 control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our 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.

We will rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with legal and regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates.

We will depend upon third parties, including independent investigators, to conduct our clinical trials under agreements with universities, medical institutions, CROs, strategic partners and others. We expect to have to negotiate budgets and contracts with CROs and trial sites, which may result in delays to our development timelines and increased costs.

We will rely heavily on third parties over the course of our clinical trials, and, as a result, will have limited control over the clinical investigators and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol and other legal, regulatory and scientific standards. Nevertheless, we are responsible for ensuring

that each of our studies is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our legal responsibilities. We and these third parties are required to comply with good clinical practice ("GCP") requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP requirements. In addition, our clinical trials must be conducted with product produced under cGMP, and in certain cases, cGTP, requirements and may require a large number of test patients.

Our failure or any failure by these third parties to comply with these requirements or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates applicable federal, state or local, as well as foreign, laws and regulations, such as the fraud and abuse or false claims laws and regulations or privacy and security laws.

Any third parties conducting our future clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether they devote sufficient time and resources to our ongoing preclinical, clinical, and nonclinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, the transition to a new CRO may result in delays, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, political unrest and global financial crises can cause extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, political unrest or additional global financial crises could result in a variety of risks to our business, including weakened demand for our products, if approved, or our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate, further political

developments and financial market conditions could adversely impact our business.

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, theft, vandalism, accidental or intentional errors, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure or accident and are not aware of any 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 discovery and 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 completed or 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.

Risks Related to Government Regulation

The regulatory approval process for our potential product candidates in the U.S., EU and other jurisdictions is currently uncertain and will be lengthy, time-consuming and inherently unpredictable and we may experience significant delays in the clinical development and regulatory approval, if any, of our product candidates.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products, including biologics, are subject to extensive regulation by the FDA in the U.S. and other regulatory authorities. We are not permitted to market any drug or biological product in the U.S. until we receive regulatory approval from the FDA. We have not previously submitted an NDA or BLA to the FDA, or similar approval filings to comparable foreign authorities. An NDA or BLA must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe and effective or, for biological products, safe, pure and potent for each desired indication. The application must also include significant information regarding the chemistry, manufacturing and controls for the product, and the manufacturing facilities must complete a successful pre-approval inspection by the FDA, or applicable foreign authority, prior to the approval or licensure of the product. We expect the novel nature of our product candidates to create further challenges in obtaining regulatory approval. For example, the FDA has not approved any nuclease edited cell therapies for in vivo or ex vivo human therapeutic use. The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any product candidates that we develop based on the completed clinical trials. Moreover, while we are not aware of any specific genetic or biomarker diagnostic tests for which regulatory approval would be necessary in order to advance any of our product candidates to clinical trials or potential commercialization, in the future regulatory agencies may require the development and approval of such tests. Accordingly, the regulatory approval pathway for such product candidates may be uncertain, complex, expensive and lengthy, and approval may not be obtained.

In addition, clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- obtaining and maintaining regulatory authorization to conduct a trial, if applicable;
- the availability of financial resources to begin and complete the planned trials;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining approval at each clinical trial site by an independent IRB;

- recruiting suitable patients to participate in a trial in a timely manner;
- having patients complete a trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol, not complying with GCP requirements or dropping out of a trial;
- addressing any patient safety concerns that arise during the course of a trial;
- addressing any conflicts with new or existing laws or regulations;

- adding new clinical trial sites; or
- manufacturing qualified materials under cGMP regulations for use in clinical trials.

Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors. Further, a clinical trial may be suspended or terminated by us, the IRBs for the institutions in which such trials are being conducted, the DSMB for such trial or the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of product candidates, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenue will be impaired. In addition, any delays in completing any clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and sale of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the U.S., including additional preclinical studies or clinical trials as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the U.S., a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we are allowed to charge for our products is also subject to approval.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets or to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Even if we receive regulatory approval of any product candidates or therapies, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, distribution, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, potency, efficacy and other post-market information, including both federal and state requirements in the U.S. and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and GCP, and in certain cases, cGTP, requirements for any clinical trials that we conduct post-approval.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to

cGMP and, in certain cases, cGTP requirements. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA or BLA, other marketing applications, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase IV clinical trials and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements

to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with legal or regulatory requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA may seek to impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the U.S. market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability. The policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. 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 and legal compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

The policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the U.S. or abroad. For example, certain policies of the current or future U.S. administration may impact our business and industry. Namely, the current administration has taken, or may take, several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking and issuance of guidance. On January 30, 2017, the U.S. president issued an executive order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In guidance issued by the Office of Information and Regulatory Affairs within OMB on April 5, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents, and on September 8, 2017, the FDA published

notices in the Federal Register soliciting broad public comment to identify regulations that could be modified in compliance with these Executive Orders. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Healthcare cost control initiatives, including healthcare legislative reform measures, may have a material adverse effect on our business and results of operations.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the U.S. and certain foreign jurisdictions, there have been, and are expected to continue to be, a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In the U.S., however, significant uncertainty exists regarding the provision and financing of health care because the current administration and federal legislators have publicly declared their intention to significantly modify the current legal and regulatory framework for the health care system but details have not been agreed upon or disclosed.

Current legislation at the U.S. federal and state levels seeks to reduce healthcare costs and improve the quality of healthcare. In March 2010, the Affordable Care Act was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical and biotechnology industry. The Affordable Care Act, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extends the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjects manufacturers to new annual fees and taxes for certain branded prescription drugs and biologic agents and provides incentives to programs that increase the federal government's comparative effectiveness research. At this time, the full effect that the Affordable Care Act would have on our business remains unclear. Further, significant uncertainty exists regarding the future scope and effect of the Affordable Care Act because the current administration and federal legislators have publicly declared their intention to significantly modify or repeal the legislation. We cannot predict the ultimate form or timing of any modification to, or repeal of, the Affordable Care Act or the effect that such modification or repeal would have on our business. Public announcements by the U.S. administration and members of the U.S. Congress have emphasized the administration's significant interest in pursuing prompt healthcare reform. Such reform efforts and any resulting changes to the Affordable Care Act, or related regulations and laws, could impact our ability to sell our products profitably.

Other legislative changes relevant to the health care system have been adopted in the U.S. since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012, was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals and other treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In December 2017, the U.S. president signed into law the Tax Cuts and Jobs Act ("TCJA"), which among other things, repealed the Affordable Care Act's requirement that all Americans under age 65 have health insurance or pay a financial payment. These laws may result in additional reductions in Medicare, Medicaid and other healthcare funding, or insured patients generally, which could have a material adverse effect on our future, potential customers and, accordingly, our financial operations.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. As indicated previously, significant uncertainty exists regarding the future scope and effect of current health care legislation and regulations because the current administration and federal legislators have publicly declared their

intention to significantly modify or repeal the current legislative framework. We cannot predict the initiatives that may be adopted in the future, any of which could limit or modify the amounts that foreign, federal and state governments as well as private payors, including patients, will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

The continuing efforts of governments, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls could harm our business, financial conditions and prospects and may adversely affect:

- the demand for or utilization of our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;

- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes, fees and rebates that we are required to pay; and
- the availability of capital.

Any denial in coverage or reduction in reimbursement from Medicare or other government programs, including state and foreign programs, may result in a similar denial or reduction in payments from private payors, which may adversely affect our future profitability.

Our employees, independent contractors, clinical investigators, CROs, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of non-compliance, fraud, misconduct or other illegal activity by our employees, independent contractors, clinical investigators, CROs, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to: comply with federal and state laws and those of other applicable jurisdictions; provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies; comply with manufacturing standards; comply with federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the U.S. and similar foreign privacy or fraudulent misconduct laws; or report financial information or data accurately; or disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the U.S., our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with clinical investigators and research patients, as well as proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare products and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, including promotion and marketing of off-label uses of our products, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person or government 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, including the imposition of significant fines or other sanctions.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, physician payment transparency laws, health information privacy and security laws and anti-corruption laws. If we are unable to comply, or have not fully complied, with such laws or their relevant foreign counterparts, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the U.S., our operations may be directly, or indirectly through our future, potential customers and third-party payors, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws or their relevant foreign counterparts may impact, among other things, our proposed sales, marketing, and education programs and our relationships with healthcare providers, physicians and other parties through which we market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to patient privacy regulation by the

federal government and the states in the U.S. as well as other jurisdictions. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. 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;
- federal civil and criminal false claims laws and civil monetary penalties laws, including the civil False Claims Act, which impose criminal and civil penalties on individuals or entities for, among other things, knowingly presenting, or causing to be presented to the U.S. federal government, claims for payment or approval that are false or fraudulent or knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which imposes criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services. 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;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;
- the U.S. federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act," created under the Affordable Care Act, and their implementing regulations, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the Centers for Medicare and Medicaid Services, information related to payments or other transfers of value made to physicians, other healthcare providers, and teaching hospitals, as well as ownership and investment interests held by physicians, other healthcare providers, and their immediate family members;
- the Foreign Corrupt Practices Act ("FCPA") and other laws which prohibit improper payments or offers of payments to foreign governments and their officials and political parties by U.S. persons and issuers as defined by the statute for the purpose of obtaining or retaining business; and
- the Federal Food, Drug and Cosmetic Act, which prohibits, among other things, the commercialization of adulterated or misbranded of drugs and medical devices and the Public Health Service Act, which prohibits, among other things, the commercialization of biological products unless a biologics license is in effect.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payor.

Because of the breadth of these laws and the limited 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. In addition, recent health care reform legislation has strengthened these laws. For example, the Affordable Care Act, among other things, amends the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes. As a result of such amendment, a person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation. Moreover, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

The increasingly global nature of our business operations subjects us to domestic and foreign anti-bribery and anti-corruption laws and regulations, such as the FCPA. Activities conducted in jurisdictions outside of the U.S. create the risk of unauthorized payments or offers of payments that are prohibited under the FCPA or comparable laws and regulations. It is our policy to implement safeguards to discourage these practices by our employees. However, these safeguards may ultimately prove ineffective, and our employees, consultants, and agents may engage in conduct for which we might be held responsible. Violations of the FCPA may result in severe criminal or civil sanctions, and we may be subject to other liabilities, which could negatively affect our business, operating results and financial condition.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations as well as other domestic and foreign legal requirements will involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other U.S. federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the U.S. will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If we fail to comply with environmental, health and safety, and laboratory animal welfare laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous federal, state and local environmental, health and safety, and laboratory animal welfare laws and regulations. These legal requirements include those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes as well as those which regulate the care and use of animals in research. Our operations will involve research using research animals and the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also may produce hazardous waste products. We generally anticipate contracting 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 maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety, and laboratory animal welfare 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.

Risks Related to Our Intellectual Property

Third-party claims of intellectual property infringement against us, our licensors or our collaborators may prevent or delay our product discovery and development efforts.

Our commercial success depends in part on our avoiding infringement of the valid patents and proprietary rights of third parties.

Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our product candidates. As industry, government, academia and other biotechnology and pharmaceutical research expands and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. We cannot guarantee that our technology, future product candidates or the use of such product candidates do not infringe third-party patents. It is also possible that we have failed to identify relevant third-party patents or applications. Because patent rights are granted jurisdiction-by-jurisdiction, our freedom to practice certain technologies, including our ability to research, develop and commercialize our product candidates, may differ by country.

Third parties may assert that we infringe their patents or that we are otherwise employing their proprietary technology without authorization, and may sue us. There may be third-party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover product candidates we discover and develop. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies or the manufacture, use or sale of our product candidates infringes upon these patents. If any such third-party patents were held by a court of competent jurisdiction to cover our technologies or product candidates, the holders of any such patents may be able to block our ability to commercialize the applicable product candidate unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business.

Third parties may seek to claim intellectual property rights that encompass or overlap with intellectual property that we own or license from others. Legal proceedings may be initiated to determine the scope and ownership of these rights, and could result in our loss of rights, including injunctions or other equitable relief that could effectively block our ability to further develop and commercialize our product candidates. For example, through our 2014 license agreement with Caribou, we sublicense the rights of the Regents of the University of California and the University of Vienna (collectively, UC/Vienna) to a worldwide patent portfolio that covers methods of use and compositions relating to engineered CRISPR/Cas9 systems for, among other things, cleaving or editing DNA and altering gene product expression in various organisms, including eukaryotic cells. We sublicense the UC/Vienna rights to this portfolio for human therapeutic, prophylactic and palliative uses, including companion diagnostics, except for anti-fungal and anti-microbial uses. This patent portfolio to-date includes, for example, one allowed and multiple allowable patent applications in the U.S., as well as granted patents from the European Patent Office, the United Kingdom’s Intellectual Property Office, the German Patent and Trade Mark Office, Australia’s Intellectual Property agency and China’s Intellectual Property Office. Because UC/Vienna co-own this portfolio with Dr. Emmanuelle Charpentier (from whom we do not have sublicense rights), we refer to this co-owned worldwide patent portfolio as the UC/Vienna/Charpentier patent family. The Broad Institute, Massachusetts Institute of Technology, the President and Fellows of Harvard College and the Rockefeller University (collectively, the Broad Institute patent family) co-own patents and patent applications that also claim certain aspects of CRISPR/Cas9 systems to edit genes in eukaryotic cells, including human cells. Because the respective owners of a UC/Vienna/Charpentier patent application

and the Broad Institute patent family both allege owning intellectual property claiming overlapping aspects of CRISPR/Cas9 systems and methods to edit genes in eukaryotic cells, including human cells, our ability to market and sell CRISPR/Cas9-based human therapeutics may be adversely impacted depending on the scope and actual ownership over the inventions claimed in the competing patent portfolios. In January 2016, an interference proceeding was declared in the U.S. Patent and Trademark Office ("USPTO") between the claims from one UC/Vienna/Charpentier patent application we sublicense through Caribou and certain U.S. patents and one application of the Broad Institute patent family to determine which set of inventors invented first and, thus, is entitled to patents on the invention in the U.S. In February 2017, the Patent Trial and Appeal Board ("PTAB") dismissed the interference proceeding finding that the respective patent claims involved in the interference were distinct such that they did not meet the legal requirement to proceed with the interference. The PTAB did not make any decision regarding inventorship or priority, and therefore ownership, of the inventions claimed by the patents and applications at issue. UC/Vienna/Charpentier appealed to the U.S. Court of Appeals for the Federal Circuit seeking a review and reversal of the PTAB's decision to terminate the interference.

The Federal Circuit conducted the hearing on the appeal on April 30, 2018, and the Company expects a decision subsequent to such hearing. In addition, several other parties also claim and are seeking intellectual property rights that could overlap with aspects of the CRISPR/Cas9 inventions covered by the UC/Vienna/Charpentier patent portfolio, which could result in other legal proceedings, including interference proceedings, to determine the ownership and scope of the inventions claimed by each party including UC/Vienna/Charpentier. If UC/Vienna/Charpentier are unable to prevail in their inventorship claims or if the scope of their claims is narrowed through these legal proceedings, then we could be prevented from developing and commercializing all or some of our products candidates unless we can obtain rights to the third-parties' intellectual property, or avoid or invalidate it.

Third parties could also assert patent rights against us to seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize product candidates. For example, the Broad Institute or other third-parties that own issued patents, including patents claiming aspects of the CRISPR-Cas9 technology, could seek to assert such patents against us claiming that our activities, including those relating to the CRISPR-Cas9 technology, infringe their respective patents. Defense of these or similar claims, regardless of their merit, would involve substantial legal expense, would be a substantial diversion of management and other employee resources from our business and may impact our reputation. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for any adjudicated willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. In that event, we may be unable to further develop and commercialize our product candidates, which could harm our business significantly.

Third parties asserting their patent rights against us may seek and obtain injunctive or other equitable relief, which could effectively limit or block our ability to further develop and commercialize our product candidates. If we are found to infringe a third party's valid intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and 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 access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing, manufacturing or importing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing one or more of our product candidates, force us to redesign our infringing products or force us to cease some or all of our business operations, any of which could materially harm our business and could prevent us from further developing and commercializing our proposed future product candidates thereby causing us significant harm. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

Intellectual property owned by third parties relating to CRISPR/Cas9 or other related technologies necessary to develop, manufacture and commercialize viable CRISPR/Cas9 therapeutics – such as compositions of the products or components, methods of treatment, delivery technologies, chemical modifications, and analytical and manufacturing methods – could adversely impact our ability to ultimately market and sell products. Third parties may own intellectual property, including patents, that cover all or aspects of our technologies and potential products, and may be necessary for us to develop or commercialize viable products. If we are unable to successfully license, avoid or challenge such third-party intellectual property, we may not be able to develop and commercialize viable products in all or certain jurisdictions. In addition, if the intellectual property covering our products or technologies that we own or license were to be legally impaired or lost, we may be unable to realize sufficient financial returns to support the development or commercialization of our products. For additional information regarding the risks that may apply to our and our licensors' intellectual property rights, see the section entitled "Risks Related to Our Intellectual Property" appearing elsewhere in this report for more information.

Under our license agreement with Caribou, we sublicense a patent family from The Regents of the University of California and the University of Vienna that is co-owned by Dr. Emmanuel Charpentier. The outcome of recent proceedings, as well as potential future proceedings, related to this patent family may affect our ability to utilize the intellectual property sublicensed under our license agreement with Caribou.

The Broad Institute patent family includes issued patents in the U.S. and Europe that purport to cover certain aspects of the CRISPR/Cas9 gene editing platform for use on eukaryotic cells, including human cells. On January 11, 2016, the PTAB declared an interference proceeding between certain patents and a patent application of the Broad Institute patent family and one UC/Vienna/Charpentier patent application to determine, based on priority of invention, whether the contested inventions belong either to UC/Vienna/Charpentier or to the Broad Institute in the U.S. This interference proceeding was discontinued by

the PTAB in February 2017 without any finding regarding inventorship or priority. In discontinuing the interference proceeding, the PTAB found that the claim sets presented by the two parties were "patentably distinct" from each other and, thus, did not meet the statutory requirements for continuing the proceeding. In April 2017, UC/Vienna/Charpentier appealed to the U.S. Court of Appeals for the Federal Circuit seeking a review and reversal of the PTAB's decision to terminate the interference, and briefing by the parties has been completed. Unless otherwise resolved, the Federal Circuit is expected to render a decision after an oral hearing, which was held on April 30, 2018. In addition, UC/Vienna/Charpentier continue to prosecute other patent claims covering the CRISPR/Cas9 inventions, which could also result in allowable or issued patents in the U.S. Certain of the claims being prosecuted by UC/Vienna/Charpentier, if found allowable by the USPTO, could lead to interference proceedings against patents or patent applications owned by other parties, including the Broad Institute patent family, with respect to certain claims expressly relating to the use of CRISPR/Cas9 in eukaryotic cells. We cannot be certain which of these results, if any, will actually occur. Further, the effects that any such results may have on us and our intellectual property position, including whether UC/Vienna/Charpentier will ultimately be successful in prosecuting to issuance a patent covering the CRISPR/Cas9 system that we are able to use under our license agreement with Caribou, are currently unknown. The Broad could seek to assert its issued patents against us based on our CRISPR/Cas9-based activities, including commercialization. Defense of these claims, regardless of their merit, would involve substantial litigation expense, would be a substantial diversion of management and other employee resources from our business and may impact our reputation. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. In that event, we could be unable to further develop and commercialize our product candidates, which could harm our business significantly.

In addition, other third parties, such as Vilnius University, ToolGene, Inc., MilliporeSigma (a subsidiary of Merck KGaA) and Harvard University, filed patent applications claiming CRISPR/Cas9-related inventions around or within a year after the UC/Vienna/Charpentier application was filed and may allege that they invented one or more of the inventions claimed by UC/Vienna/Charpentier before UC/Vienna/Charpentier. If the USPTO deems the scope of the claims of one or more of these parties to sufficiently overlap with the allowable claims from the UC/Vienna/Charpentier application, the USPTO could declare other interference proceedings to determine the actual inventor of such claims. In addition, UC/Vienna/Charpentier or the other third parties could seek judicial review of their inventorship claims. If UC/Vienna/Charpentier fail in defending their inventorship priority on any of these claims, we may lose valuable intellectual property rights, such as the exclusive right to use, such intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, any disputes could result in substantial costs and be a distraction to management and other employees.

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

We may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor or other claims challenging the inventorship of our patents or ownership of our intellectual property (including patents and intellectual property that we in-license). For example, the UC/Vienna/Charpentier patent family that is covered by our license agreement with Caribou is co-owned by UC/Vienna and Dr. Charpentier, and our sublicense rights are derived from the first two co-owners and not from Dr. Charpentier. Therefore, our rights to these patents are not exclusive and third parties, including competitors, may have access to intellectual property that is important to our business. In addition, we may have inventorship disputes arise from conflicting obligations of collaborators, consultants or others who are involved in developing our technology and product candidates. Litigation or other legal proceedings may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are

successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We depend on intellectual property licensed from third parties and termination or modification of any of these licenses could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others, including Caribou and Novartis. Any termination of these licenses, loss by our licensors of the rights they receive from others, or a finding that such intellectual property lacks legal effect, could result in the loss of significant rights and could harm our ability to commercialize any product candidates.

Disputes have and may arise between us and our licensors, our licensors and their licensors, or us and third parties that co-own intellectual property with our licensors or their licensors, regarding intellectual property subject to a license agreement, including those relating to:

- the scope of rights, if any, granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology, products and processes infringe on, or derive from, intellectual property of the licensor that is not subject to the license agreement;
- whether our licensor or its licensor had the right to grant the license agreement, or whether they are compliant with their contractual obligations to their respective licensor(s);
- whether third parties are entitled to compensation or equitable relief, such as an injunction, for our use of the intellectual property without their authorization;
- our right to sublicense patent and other rights to third parties, including those under collaborative development relationships;
- whether we are complying with our obligations with respect to the use of the licensed technology in relation to our development and commercialization of product candidates;
- our involvement in the prosecution, defense and enforcement of the licensed patents and our licensors' overall patent strategy;
- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us and our partners; and
- the amounts of royalties, milestones or other payments due under the license agreement.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, or are insufficient to provide us the necessary rights to use the intellectual property, we may be unable to successfully develop and commercialize the affected product candidates. If we or any such licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer.

We depend, in part, on our licensors to file, prosecute, maintain, defend and enforce patents and patent applications that are material to our business.

Patents relating to our product candidates are controlled by certain of our licensors or their respective licensors. Each of our licensors or their licensors generally has rights to file, prosecute, maintain and defend the patents we have licensed from such licensor. If these licensors or any future licensees and in some cases, co-owners from which we do not yet have licenses, having rights to file, prosecute, maintain, and defend our patent rights fail to adequately conduct these activities for patents or patent applications covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using or selling competing products. We cannot be certain that such activities by our licensors or their respective licensors have been or will be conducted in compliance with applicable laws and regulations or in our best interests, or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with our licensors, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and, even if we are permitted to pursue such enforcement or defense, we cannot ensure the cooperation of our licensors or, in some cases, other necessary parties, such as the co-owners of the intellectual property from which we have not yet obtained a license. We cannot be certain that our licensors or their licensors, and in some cases, their respective co-owners, will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. For example, with respect to our sublicensed rights from Caribou to UC/Vienna/Charpentier intellectual property, UC retained the right to control the prosecution, enforcement and defense of this intellectual property in its license agreement with Caribou and, pursuant to an Invention Management Agreement, shares these responsibilities with CRISPR Therapeutics and, under certain circumstances, ERS, as the designated managers of the intellectual property. For these reasons, UC may be unable or unwilling to prosecute certain patent claims that would be best for

our product candidates, or enforce its patent rights against infringers of the UC/Vienna/Charpentier patent family.

Even if we are not a party to legal actions or other disputes involving our licensed intellectual property, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. In addition, even when we have the right to control patent prosecution of licensed patents and patent applications, enforcement of licensed patents, or defense of claims asserting the invalidity of those patents, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to or after our assuming control.

We may not be successful in obtaining or maintaining necessary rights to product components and processes or other technology for our product development pipeline.

The growth of our business will likely depend in part on our ability to acquire or in-license additional proprietary rights. For example, our programs may involve additional product candidates, delivery systems or technologies that may require the use of additional proprietary rights held by third parties. Our ultimate product candidates may also require specific modifications or formulations to work effectively and efficiently. These modifications or formulations may be covered by intellectual property rights held by others. We may be unable to acquire or in-license any relevant third-party intellectual property rights that we identify as necessary or important to our business operations.

Additionally, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

The licensing and acquisition of third-party intellectual property rights is a competitive practice and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

If we are unable to successfully obtain rights to valid third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates, or asserting and defending our intellectual property rights that protect our products and technologies.

We anticipate that we will file additional patent applications both in the U.S. and in other countries, as appropriate. However, we cannot predict:

- if and when any patents will issue;
- the scope, degree and range of protection any issued patents will afford us against competitors, including whether third parties will find ways to invalidate or otherwise circumvent our patents;
- whether others will apply for or obtain patents claiming aspects similar to those covered by our patents and patent applications;
- whether certain governments will appropriate our intellectual property rights and allow competitors to use them; or

- whether we will need to initiate litigation or administrative proceedings to assert or defend our patent rights, which may be costly whether we win or lose.

Composition of matter patents for biological and pharmaceutical products are generally considered to be the strongest form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. We cannot be certain, however, that any claims in our pending or future patent applications covering the composition of matter of our product candidates will be considered patentable by the USPTO or by patent offices in foreign countries, or that

the claims in any of our ultimately issued patents will be considered valid and enforceable by courts in the U.S. or foreign countries. Method of use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products “off-label” for those uses that are covered by our method of use patents. Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The strength of patents in the biotechnology and pharmaceutical field can be uncertain, and evaluating the scope of such patents involves complex legal and scientific analyses. The patent applications that we own or in-license may fail to result in issued patents with claims that cover any product candidates or uses thereof in the U.S. or in other foreign countries.

Further, the patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner, or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. We may also require the cooperation of our licensors or other necessary parties, such as the co-owners of the intellectual property from which we have not yet obtained a license, in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. and we may fail to seek or obtain patent protection in all major markets. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we will be unable to know with certainty whether we were the first to make any inventions claimed in any patents or patent applications, or that we were the first to file for patent protection of such inventions, nor can we know whether those from whom we license patents were the first to make the inventions claimed or were the first to file.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U.S. and abroad. There is a substantial amount of litigation as well as administrative proceedings for challenging patents, including interference, derivation, and reexamination proceedings before the USPTO and oppositions and other comparable proceedings in foreign jurisdictions, involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, and we expect this to be true for the CRISPR/Cas9 space as well. For example, a number of third parties have filed oppositions challenging the validity, and seeking the revocation, of the CRISPR/Cas9 genome editing patents granted to UC/Vienna/Charpentier by the European Patent Office to date.

In addition, since the passage of the America Invents Act in 2013, U.S. law also provides for other procedures to challenge patents, including inter partes reviews and post-grant reviews, that add uncertainty to the possibility of challenge to our developed or licensed patents and patent applications in the future. Furthermore, for U.S. applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. See above Third-party claims of intellectual property infringement against us, our licensors or our collaborators may prevent or delay our product discovery and development efforts.

Such challenges may result in 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 practice the invention or stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing their products to avoid being covered by our claims. If the breadth or strength of protection provided by the patent applications we hold is threatened, this could dissuade companies from collaborating with us to develop, and could threaten our ability to commercialize, product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market product candidates under patent protection would be reduced. Because patent applications in the U.S. and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates.

Our pending and future patent applications or the patent applications that we obtain rights to through in-licensing arrangements may not result in patents being issued which protect our technology or future product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Litigation or other administrative proceedings challenging our intellectual property, including interferences, derivation, reexamination, inter partes reviews and post-grant reviews, may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. Furthermore, there could be public announcement of the results of hearings, motions or other interim proceedings or developments in any proceeding challenging the issuance, scope, validity and enforceability of our developed or licensed intellectual property. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Any of these potential negative developments could impact the scope, validity, enforceability or commercial value of our patent rights and, as a result, have material adverse effect on our business, financial condition, results of operations or prospects.

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent. We also utilize proprietary processes for which patents are difficult to enforce. In addition, other elements of our product discovery and development processes involve proprietary know-how, information, or technology that is not covered by patents. Trade secrets, however, may be difficult to protect. We seek to protect our proprietary processes, in part, by entering into confidentiality agreements with our employees, consultants, outside scientific advisors, contractors, and collaborators. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, outside scientific advisors, contractors, and collaborators might intentionally or inadvertently disclose our trade secret information to competitors. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results, and financial condition.

We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.

We have limited intellectual property rights outside the U.S. Filing, prosecuting, maintaining and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can have a different scope and strength than do those in the U.S. In addition, the laws of some foreign countries, such as China, Brazil, Russia, India, and South Africa, do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the U.S. These products may compete with our products and our patents or other intellectual property rights may not be effective or adequate to prevent them from competing. In addition, in jurisdictions outside the U.S., a license may not be enforceable unless all the owners of the intellectual property agree or

consent to the license. Further, patients may choose to travel to countries in which we do not have intellectual property rights or which do not enforce these rights to obtain the products or treatment from competitors in such countries.

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

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

Competitors may infringe our patents or the patents of our licensors. To cease such infringement or unauthorized use, we may be required to file patent infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding or a declaratory judgment action against us, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Interference or derivation proceedings provoked by third parties or brought by the USPTO may be necessary to determine the priority of inventions with respect to, or the correct inventorship of, our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Litigation, interference or derivation proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees.

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

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or before the USPTO or comparable foreign authority.

If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid

or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the U.S. or other jurisdictions, even outside the context of litigation. Such mechanisms include re-examination, inter partes review, post-grant review and equivalent proceedings in foreign jurisdictions, such as opposition or derivation proceedings. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity, unpatentability and/or

unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies as well as academic research institutions. We may be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. Litigation may be necessary to defend against these claims, which could result in money damages or a judicial order prohibiting the use of certain intellectual property. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. Although an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We may be required to pay certain milestones and royalties under our license agreements with third-party licensors.

Under our current and future license agreements, we may be required to pay milestones and royalties based on our revenues from sales of our products utilizing the technologies licensed or sublicensed from third parties, including Caribou, Novartis and Regeneron, and these royalty payments could adversely affect the overall profitability for us of any products that we may seek to commercialize. In order to maintain our license rights under these license agreements, we will need to meet certain specified milestones, subject to certain cure provisions, in the development of our product candidates and in the raising of funding. In addition, these agreements contain diligence milestones and we may not be successful in meeting all of the milestones in the future on a timely basis or at all. We will need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our products covered under our license agreements. Delay or failure by these third parties could adversely affect the continuation of our license agreements with their third-party licensors.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among

potential partners or future, potential customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Risks Related to Our Common Stock

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

In May 2016, we closed our initial public offering. Prior to this offering, there was no public market for our common stock. Although we have completed our initial public offering and shares of our common stock are listed and trading on the Nasdaq Global Market, an active trading market for our shares may not be sustained. If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at or above the prices at which they acquired their shares or sell their shares at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The price of our common stock historically has been volatile, which may affect the price at which you could sell any shares of our common stock.

The market price for our common stock historically has been highly volatile and could continue to be subject to wide fluctuations in response to various factors. This volatility may affect the price at which you could sell the shares of our common stock, and the sale of substantial amounts of our common stock could adversely affect the price of our common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including:

- the success of our or competing products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- developments or disputes concerning patent applications, issued patents or other intellectual property rights;
- regulatory or legal developments in the U.S. and other countries;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- 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;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell 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.

In addition, companies trading in the stock market in general, and in the Nasdaq Global Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management’s attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Our principal stockholders and management own a significant percentage of our stock and, if they choose to act together, will be able to control or exercise significant influence over matters subject to stockholder approval.

As of March 31, 2018, our executive officers, directors, five percent or greater stockholders and their affiliates beneficially own approximately 43.6% of our outstanding voting stock. These stockholders may have the ability to influence us through their ownership positions. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We have broad discretion over the use of our cash and cash equivalents and may not use them effectively.

Our management has broad discretion to use our cash and cash equivalents to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending our use to fund operations, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

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

The Company will need additional capital in the future to continue our planned operations in addition to the proceeds we received from our initial public offering in May 2016 and follow-on public offering in November 2017. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to the Company’s existing stockholders, and new investors could gain rights superior to our existing stockholders.

In addition, sales of a substantial number of shares of our outstanding common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Persons who were our stockholders prior to our IPO continue to hold a substantial number of shares of our common stock that many of them are now able to sell in the public market. Significant portions of these shares are held by a relatively small number of stockholders. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us difficult, limit attempts by our stockholders to replace or remove our current management and adversely affect our stock price.

Provisions of our certificate of incorporation and by-laws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our stock. Among other things, the certificate of incorporation and by-laws:

- permit the board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide the board of directors into three classes;
- provide that a director may only be removed from the board of directors by the stockholders for cause;

- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders, and may not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner, and meet specific requirements as to the form and content of a stockholder's notice;
- prevent cumulative voting rights (therefore allowing the holders of a plurality of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- require that, to the fullest extent permitted by law, a stockholder reimburse us for all fees, costs and expenses incurred by us in connection with a proceeding initiated by such stockholder in which such stockholder does not obtain a judgment on the merits that substantially achieves the full remedy sought;
- provide that special meetings of our stockholders may be called only by the chairman of the board, our chief executive officer (or president, in the absence of a chief executive officer) or by the board of directors; and
- provide that stockholders will be permitted to amend the bylaws only upon receiving at least two-thirds of the total votes entitled to be cast by holders of all outstanding shares then entitled to vote generally in the election of directors, voting together as a single class.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any "interested" stockholder for a period of three years following the date on which the stockholder became an "interested" stockholder.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our by-laws, any action to interpret, apply, enforce, or determine the validity of our certificate of incorporation or bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provision contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an "emerging growth company" under applicable SEC regulations, we incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 ("Section 404"), we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we are not required to include an attestation report on internal control over financial reporting issued by our

independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as

appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts may not publish an adequate amount of research on the Company, which may negatively impact the trading price for our stock. In addition, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. Further, if our operating results fail to meet the forecasts of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of the Company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We could be subject to significant legal proceedings which may adversely affect our results of operations or financial condition.

We are subject to the risk of litigation, derivative claims, securities class actions, regulatory and governmental investigations and other proceedings, including proceedings arising from investor dissatisfaction with us or our performance. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If any claims were brought against us and resulted in a finding of substantial legal liability, the finding could materially adversely affect our business, financial condition or results of operations or cause significant reputational harm to us, which could seriously adversely impact our business. Allegations of improper conduct by private litigants or regulators, regardless of veracity, may harm our reputation and adversely impact our ability to grow our business. If we face such litigation, it could result in substantial costs and a diversion of management’s attention and resources, which could harm our business.

Changes in tax law may adversely affect our business and financial condition.

The laws and rules dealing with U.S. federal, state and local income taxation are routinely being reviewed and modified by governmental bodies, officials and regulatory agencies, including the Internal Revenue Service and the U.S. Treasury Department. Since the Company was founded in 2014, many such changes have been made and changes are likely to continue to occur in the future. For example, in December 2017, the U.S. president signed into law the TCJA that significantly reforms the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and effectuates the migration from a “worldwide” system of taxation to a territorial system. Our net deferred tax assets and

liabilities have been revalued at the newly enacted U.S. corporate rate. The impact of this tax reform is uncertain and could be adverse. It cannot be predicted whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or issued, that could result in an increase in our or our shareholders' tax liability.

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. As of December 31, 2017, we had federal and state net operating loss carryforwards of $36.7 million and $27.8 million, respectively, which begin to expire in 2034. As of December 31, 2017,

we had federal and state research and development tax credit carryforwards of approximately $3.4 million and $2.5 million, which begin to expire in 2034 and 2030, respectively. Our net deferred tax assets and liabilities have been revalued at the newly enacted U.S. corporate rate. Under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. We may have experienced ownership changes in the past and may experience ownership changes in the future as a result of this offering and/or subsequent shifts in our stock ownership (some of which shifts are outside our control). As a result, if we earn net taxable income, our ability to use our pre-change NOLs to offset such taxable income could be subject to limitations. Similar provisions of state tax law may also apply. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes. Under the TCJA, net operating losses generated after December 31, 2017 are not subject to expiration.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

None.

Item 6. Exhibits

The following exhibits are incorporated by reference or filed as part of this report.

| | |
|---|---|
| 10.1 | Form of Amended and Restated Employment Agreement (1) |
| 31.1 | Certification of Chief Executive Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. (2) |
| 31.2 | Certification of Chief Financial Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. (2) |
| 32.1 | Certifications pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002, by John M. Leonard, M.D., President and Chief Executive Officer of the Company, and Graeme Bell, Executive Vice President, Chief Financial Officer of the Company. (2) |
| 101.INS | XBRL Instance Document. |
| 101.SCH | XBRL Taxonomy Extension Schema Document. |
| 101.CAL | XBRL Taxonomy Extension Calculation Linkbase Document. |
| 101.DEF | XBRL Taxonomy Extension Definition Linkbase Document. |
| 101.LAB | XBRL Taxonomy Extension Label Linkbase Document. |
| 101.PRE | XBRL Taxonomy Extension Presentation Linkbase Document. |

(1) Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-37766) filed with the Securities and Exchange Commission on April 17, 2018.
(2) Filed with this Form 10-Q.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Dated: May 1, 2018

INTELLIA THERAPEUTICS, INC.

By: /s/ John M. Leonard
John M. Leonard, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

By: /s/ Graeme Bell
Graeme Bell
Executive Vice President, Chief Financial Officer
(Principal Financial and Accounting Officer)