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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549**

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**FORM 10-Q**

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(Mark One)

**QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended September 30, 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: 001-38520

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**MeiraGTx Holdings plc**

(Exact Name of Registrant as Specified in its Charter)

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Cayman Islands  
(State or other jurisdiction of  
incorporation or organization)

Not applicable  
(I.R.S. Employer  
Identification No.)

430 East 29th Street, 10th Floor  
New York, NY  
(Address of principal executive offices)

10016  
(Zip Code)

Registrant's telephone number, including area code: (646) 490-2965

Not Applicable

(Former name, former address, and former fiscal year, if changed since last report)

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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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit 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 the 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

Small 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

As of October 31, 2018, the registrant had 27,386,632 ordinary shares, \$0.00003881 par value per share, outstanding.



## **Forward-Looking Statements**

This Quarterly Report on Form 10-Q contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this Quarterly Report that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding product pipeline, anticipated product benefits, goals and strategic priorities, product candidate development, growth expectations or targets and pre-clinical and clinical data, as well as statements that include the words “expect,” “intend,” “plan,” “believe,” “project,” “forecast,” “estimate,” “may,” “should,” “anticipate” and similar statements of a future or forward-looking nature. These forward-looking statements are based on management’s current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the important factors discussed under Item 1A. “Risk Factors” in this Quarterly Report. These and other important factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this Quarterly Report. Any such forward-looking statements represent management’s estimates as of the date of this Quarterly Report. While we may elect to update such forward-looking statements at some point in the future, unless required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. Thus, one should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this Quarterly Report.

## **Presentation of Information**

On June 7, 2018, in connection with its initial public offering (the “IPO”), MeiraGTx Holdings plc, an exempted company incorporated under the laws of the Cayman Islands, acquired all of the issued and outstanding ordinary shares of MeiraGTx Limited pursuant to a series of reorganization transactions (the “Reorganization Transactions”). Prior to the Reorganization Transactions, MeiraGTx Holdings plc had not conducted any operations and had nominal assets and liabilities.

Unless the context otherwise requires, references in this Quarterly Report on Form 10-Q to “Meira,” “we,” “us,” “our” and “the Company” refer to (i) MeiraGTx Limited and its subsidiaries prior to the Reorganization Transactions and (ii) MeiraGTx Holdings plc and its subsidiaries upon completion of the Reorganization Transactions, as applicable.

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PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

**MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES**  
**CONDENSED CONSOLIDATED BALANCE SHEETS**

	<u>September 30,</u> <u>2018</u> (unaudited)	<u>December 31,</u> <u>2017</u>
<b>ASSETS</b>		
CURRENT ASSETS:		
Cash and cash equivalents	\$ 88,560,634	\$ 8,548,638
Prepaid expenses	2,029,327	1,961,243
Other current assets	716,737	965,233
Total Current Assets	91,306,698	11,475,114
Property and equipment, net	13,624,968	14,255,729
Security deposits	180,870	—
Restricted cash	123,376	123,376
<b>TOTAL ASSETS</b>	<b>\$ 105,235,912</b>	<b>\$ 25,854,219</b>
<b>LIABILITIES, CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' EQUITY (DEFICIT)</b>		
CURRENT LIABILITIES:		
Accounts payable	\$ 2,415,667	\$ 7,055,380
Accrued expenses	6,042,290	9,332,944
Note payable	—	1,442,009
Warrant liability	—	2,679,633
Capitalized lease obligation—current portion	29,284	30,850
Due to Kadmon	—	861,030
Total Current Liabilities	8,487,241	21,401,846
Capitalized lease obligation	12,092	34,298
Deferred rent	210,993	266,290
Other liabilities	181,515	178,419
<b>TOTAL LIABILITIES</b>	<b>8,891,841</b>	<b>21,880,853</b>
COMMITMENTS		
CONVERTIBLE PREFERRED C SHARES		
Convertible Preferred C Shares 0 and 5,005,935 outstanding at September 30, 2018 and December 31, 2017, respectively (liquidation preference of \$52,455,700 at December 31, 2017)	—	51,338,631
SHAREHOLDERS' EQUITY (DEFICIT):		
Ordinary Shares, \$0.00003881 nominal value, 1,288,327,750 authorized		
27,184,132 issued and outstanding at September 30, 2018		
8,826,190 issued and 8,714,563 issued and outstanding at December 31, 2017	1,055	342
Capital in excess of nominal value	223,868,465	20,080,713
Accumulated other comprehensive loss	(292,477)	(2,022,477)
Accumulated deficit	(127,232,972)	(65,423,843)
Total Shareholders' Equity (Deficit)	96,344,071	(47,365,265)
<b>TOTAL LIABILITIES, CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS' EQUITY (DEFICIT)</b>	<b>\$ 105,235,912</b>	<b>\$ 25,854,219</b>

See Notes to Condensed Consolidated Financial Statements

**MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES**  
**CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**  
**(unaudited)**

	For the Three-Month Period Ended September 30, 2018	For the Three-Month Period Ended September 30, 2017	For the Nine-Month Period Ended September 30, 2018	For the Nine-Month Period Ended September 30, 2017
Operating expenses:				
General and administrative	\$ 6,629,052	\$ 2,374,527	\$ 35,129,120	\$ 6,744,963
Research and development	8,109,160	6,388,227	22,827,176	16,575,129
Total operating expenses	<u>14,738,212</u>	<u>8,762,754</u>	<u>57,956,296</u>	<u>23,320,092</u>
Loss from operations	(14,738,212)	(8,762,754)	(57,956,296)	(23,320,092)
Other non-operating income (expense):				
Other income	—	—	83,075	—
Foreign currency (loss) gain	(677,488)	391,521	(2,425,488)	990,395
Change in fair value of warrant liability	—	—	(1,514,775)	—
Interest income	264	2,915	50,926	21,295
Interest expense	(9,508)	(72,736)	(46,571)	(131,756)
Net loss	(15,424,944)	(8,441,054)	(61,809,129)	(22,440,158)
Other comprehensive income (loss)	508,758	(348,338)	1,730,000	(824,252)
Comprehensive loss	<u>\$ (14,916,186)</u>	<u>\$ (8,789,392)</u>	<u>\$ (60,079,129)</u>	<u>\$ (23,264,410)</u>
Net loss	<u>\$ (15,424,944)</u>	<u>\$ (8,441,054)</u>	<u>\$ (61,809,129)</u>	<u>\$ (22,440,158)</u>
Accretion on convertible preferred C shares and warrants	—	(191,758)	(1,806,512)	(244,920)
Adjusted net loss	<u>\$ (15,424,944)</u>	<u>\$ (8,632,812)</u>	<u>\$ (63,615,641)</u>	<u>\$ (22,685,078)</u>
Basic and diluted net loss per ordinary share	<u>\$ (0.59)</u>	<u>\$ (1.00)</u>	<u>\$ (3.89)</u>	<u>\$ (2.66)</u>
Weighted-average number of ordinary shares outstanding	<u>26,340,450</u>	<u>8,607,832</u>	<u>16,355,849</u>	<u>8,536,447</u>

See Notes to Condensed Consolidated Financial Statements

**MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES**  
**CONDENSED CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED C SHARES AND SHAREHOLDERS'**  
**EQUITY (DEFICIT)**  
**AS OF SEPTEMBER 30, 2018**  
**(unaudited).**

	Convertible Preferred C Shares		Shareholders' Equity (Deficit)					Total Shareholders' Equity (Deficit)
	Shares	Amount	Ordinary Shares	Amount	Capital in Excess of Nominal Value	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	
Balance at December 31, 2017	5,005,935	\$ 51,338,631	8,826,190	\$ 342	\$ 20,080,713	\$ (2,022,477)	\$ (65,423,843)	\$ (47,365,265)
Issuance of convertible preferred C shares in connection with payables	129,419	1,356,129	—	—	—	—	—	—
Issuance of convertible preferred C shares in connection with a license agreement	13,360	140,000	—	—	—	—	—	—
Sale of convertible preferred C shares, net of issuance costs	5,425,124	56,159,119	—	—	—	—	—	—
Accretion of issuance costs on convertible preferred C shares	—	761,012	—	—	(761,012)	—	—	(761,012)
Accretion of warrants issued in connection with convertible preferred C shares	—	1,045,500	—	—	(1,045,500)	—	—	(1,045,500)
Exercise of warrants	927,594	9,720,000	—	—	4,194,408	—	—	4,194,408
Conversion of convertible preferred C shares into A ordinary shares	(11,501,432)	(120,520,391)	11,501,432	446	120,519,945	—	—	120,520,391
Sale of A ordinary shares in initial public offering, net of issuance costs of \$9,675,735	—	—	5,000,000	194	65,324,071	—	—	65,324,265
Share-based compensation	—	—	1,856,510	73	15,555,840	—	—	15,555,913
Foreign currency translation	—	—	—	—	—	1,730,000	—	1,730,000
Net loss for the nine-month period ended September 30, 2018	—	—	—	—	—	—	(61,809,129)	(61,809,129)
Balance at September 30, 2018	—	\$ —	27,184,132	\$ 1,055	\$ 223,868,465	\$ (292,477)	\$ (127,232,972)	\$ 96,344,071

See Notes to Condensed Consolidated Financial Statements

**MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES**  
**CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS**  
**(unaudited)**

	For the Nine-Month Period Ended September 30,	
	2018	2017
<b>Cash flows from operating activities:</b>		
Net loss	\$ (61,809,129)	\$ (22,440,158)
<b>Adjustments to reconcile net loss to net cash used in operating activities:</b>		
Preferred C shares issued in connection with a license agreement	137,658	—
Issuance of shares for services	—	16,875
Share-based compensation expense	15,555,913	2,019,652
Foreign currency loss (gain)	2,425,488	(990,395)
Depreciation	1,549,686	579,696
Amortization of interest on asset retirement obligation	10,918	14,202
Change in fair value of warrant liability	1,514,775	—
<b>Decrease (increase) in operating assets:</b>		
Prepaid expenses and other current assets	(112,440)	(259,757)
Security deposits	(180,980)	—
Other current assets	239,627	(959,566)
<b>Increase (decrease) in operating liabilities:</b>		
Deferred rent	(55,460)	1,184,269
Due to Kadmon	(861,030)	171,620
Accounts payable	(2,337,302)	3,850,544
Interest payable	—	—
Accrued expenses	(3,496,882)	2,467,083
<b>Net cash used in operating activities</b>	<b>(47,419,158)</b>	<b>(14,345,935)</b>
<b>Cash flows from investing activities:</b>		
Purchase of property and equipment	(2,372,622)	(8,389,156)
<b>Net cash used in investing activities</b>	<b>(2,372,622)</b>	<b>(8,389,156)</b>
<b>Cash flows from financing activities:</b>		
Payments on capitalized lease obligation	(23,772)	(16,753)
Exercise of warrants	9,720,000	—
Proceeds from the sale of ordinary shares	69,750,000	—
Issuance costs in connection with ordinary shares	(4,115,843)	—
Proceeds from the sale of convertible preferred C shares	56,849,592	7,739,574
Issuance costs in connection with convertible preferred C shares	(690,473)	(18,500)
(Payment) issuance of note payable	(1,442,009)	2,500,000
Proceeds from exercised stock options	—	9,950
<b>Net cash provided by financing activities</b>	<b>130,047,495</b>	<b>10,214,271</b>
<b>Net increase (decrease) in cash, cash equivalents and restricted cash</b>	<b>80,255,715</b>	<b>(12,520,820)</b>
Effect of exchange rate changes on cash	(243,719)	12,125
Cash, cash equivalents and restricted cash at beginning of period	8,672,014	17,930,421
Cash, cash equivalents and restricted cash at end of period	<u>\$ 88,684,010</u>	<u>\$ 5,421,726</u>
<b>Supplemental disclosure of non-cash transactions:</b>		
Fixed asset acquisition included in accounts payable and accrued expenses at end of period	\$ —	\$ 1,641,145
Issuance of convertible preferred C shares in connection with payables	\$ 1,356,129	\$ —
Conversion of convertible preferred C shares into ordinary shares	\$ 120,520,391	\$ —
Reclassification of warrant liability upon exercise of warrants	\$ 4,194,408	\$ —
Capitalized lease obligation for equipment purchase	\$ —	\$ 78,063
Issuance costs in connection with sale of ordinary shares in accrued expenses at end of period	\$ 309,892	\$ —
Issuance of ordinary shares in connection with a research agreement	\$ —	\$ 17,001
<b>Supplemental disclosure of cash flow information:</b>		
Cash paid for interest	<u>\$ 31,531</u>	<u>\$ 2,728</u>

See Notes to Condensed Consolidated Financial Statements

**MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES**  
**NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**

**1. Organization and Basis of Presentation:**

***The Company***

MeiraGTx Holdings plc (the “Company” or “Meira Holdings”), a limited company under the laws of the Cayman Islands, is a clinical-stage biotech company developing novel gene therapy treatments for a wide range of inherited and acquired disorders for which there are no effective treatments available. The Company is focused on developing therapies for ocular diseases, including rare inherited blindness as well as Xerostomia following radiation treatment for head and neck cancers and neurodegenerative diseases such as amyotrophic lateral sclerosis (“ALS”) and Parkinson’s disease (“PD”).

***Reorganization and Initial Public Offering***

We commenced operations as MeiraGTx Limited, a private limited company incorporated under the laws of England and Wales in 2015. On May 28, 2018, the Board of Directors of MeiraGTx Limited approved the Reorganization Transactions, effective June 7, 2018, pursuant to which the Board of Directors approved the transfer of the shares held by each of the MeiraGTx Limited’s shareholders for the equivalent class and number of shares issued by Meira Holdings. On June 7, 2018, the Company completed its IPO, selling 5,000,000 ordinary shares (“Ordinary Shares”) at a public offering price of \$15.00 per share, and receiving \$65.3 million in net proceeds, after deducting underwriting discounts and commissions and offering expenses payable by us.

***Reverse Share Split***

On June 7, 2018 MeiraGTx Limited’s Board of Directors and shareholders approved a 1:3.881 reverse share split. All share information presented in these financial statements and accompanying footnotes have been retroactively adjusted to reflect the decreased number of shares resulting from this action.

***Basis of Presentation***

The accompanying condensed consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (“GAAP”). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Update (“ASU”) of the Financial Accounting Standards Board (“FASB”).

***Interim Financial Statements***

The accompanying condensed consolidated financial statements have been prepared in accordance with GAAP for interim financial information and with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all the information and footnotes required by generally accepted accounting principles for complete consolidated financial statements. In the opinion of management, the condensed consolidated financial statements include all adjustments (consisting of normal recurring accruals) necessary in order to make the condensed consolidated financial statements not misleading. Operating results for the nine-month period ended September 30, 2018 are not necessarily indicative of the final results that may be expected for the year ended December 31, 2018. These unaudited condensed consolidated financial statements should be read in conjunction with the audited consolidated financial statements for the year ended December 31, 2017 and the notes thereto for the year ended December 31, 2017 included in the Company’s final prospectus that forms a part of the Company’s Registration Statement on Form S-1 (Reg. No. 333-224914), filed with the Securities and Exchange Commission (“SEC”) pursuant to Rule 424(b)(4) on June 8, 2018 (the “Prospectus”).

***Liquidity***

The Company has not generated any revenues and has not yet achieved profitable operations. There is no assurance that profitable operations, if ever achieved, could be sustained on a continuing basis. In addition, development activities, clinical and preclinical testing, and commercialization of the Company’s product candidates will require significant additional financing. Management expects to incur substantial and increasing losses in future periods. The success of the Company is subject to certain risks and uncertainties, including among others, uncertainty of product development; competition in the Company’s field of use; uncertainty of capital availability; uncertainty in the Company’s ability to enter into agreements with collaborative partners; dependence on third parties; and dependence on key personnel. The Company has not generated positive cash flows from operations, and there are no assurances that the Company will be successful in obtaining an adequate level of financing for the development and commercialization of its product candidates.

As of September 30, 2018, the Company had cash and cash equivalents in the amount of \$88,560,634, which consisted of depository accounts. The Company estimates that its cash and cash equivalents on hand at September 30, 2018 will cover its expenses into the second quarter of 2020.

### ***Risks and Uncertainties***

The Company operates in an industry that is subject to intense competition, government regulation and rapid technological change. The Company's operations are subject to significant risk and uncertainties including financial, operational, technological, regulatory and other risks, including the potential risk of business failure.

The Company's limited capital resources and operations to date have been funded primarily with the proceeds from private equity offerings and the IPO. In the future, the Company may seek to raise additional capital through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources to enable it to complete the development and potential commercialization of its product candidates.

## **2. Summary of Significant Accounting Policies and Recent Accounting Pronouncements:**

Certain of the Company's significant accounting policies are described below. All of the Company's significant accounting policies are disclosed in the notes to the audited consolidated financial statements as of and for the year ended December 31, 2017 included in the Company's Prospectus. Since the date of such financial statements, the Company has adopted the new accounting pronouncements which are disclosed further in this note.

### ***Consolidation***

The accompanying condensed consolidated financial statements include the accounts of Meira Holdings and its wholly owned subsidiaries:

MeiraGTx Limited, a limited company under the laws of England and Wales ("Meira Limited");  
MeiraGTx, LLC, a Delaware corporation ("Meira LLC");  
BRI-Alzan, Inc., a Delaware corporation ("BRI-Alzan");  
MeiraGTx B.V., a Netherlands corporation ("Meira BV");  
MeiraGTx UK II Limited, ("Meira UK II"), a limited company under the laws of England and Wales; and  
MeiraGTx UK Limited ("Meira UK"), a limited company under the laws of England and Wales.

All intercompany balances and transactions between the consolidated companies have been eliminated in consolidation.

### ***Use of Estimates***

Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these condensed consolidated financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes and management must select an amount that falls within that range of reasonable estimates. This process may result in actual results differing materially from those estimated amounts used in the preparation of the condensed consolidated financial statements if these results differ from historical experience, or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made. In preparing these condensed consolidated financial statements, management used significant estimates in the following areas, among others: valuation of A ordinary shares ("A Ordinary Shares") issued prior to the Company's initial public offering, for the acquisition of assets, the accounting for research and development costs, warrants, share-based compensation, asset retirement obligations and accrued expenses.

### ***Fair Value Measurements***

Fair value is defined as the price that would be received upon sale of an asset or paid upon transfer of a liability in an orderly transaction between market participants at the measurement date and in the principal or most advantageous market for that asset or liability. The fair value should be calculated based on assumptions that market participants would use in pricing the asset or liability, not on assumptions specific to the entity. In addition, the fair value of liabilities should include consideration of non-performance risk including our own credit risk.

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The Company follows ASC Topic 820, *Fair Value Measurements and Disclosures*, or ASC 820, for application to financial assets and liabilities. In addition to defining fair value, the standard expands the disclosure requirements around fair value and establishes a fair value hierarchy for valuation inputs. The hierarchy prioritizes the inputs into three levels based on the extent to which inputs used in measuring fair value are observable in the market. Each fair value measurement is reported in one of the three levels which are determined by the lowest level input that is significant to the fair value measurement in its entirety. These levels are:

- Level 1: Observable inputs such as quoted prices in active markets for identical assets the reporting entity has the ability to access as of the measurement date;
- Level 2: Inputs, other than the quoted prices in active markets, that are observable either directly or indirectly; and
- Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

The table below represents the values of the Company's financial assets and liabilities that are required to be measured at fair value on a recurring basis:

Description	Fair Value Measurement Using:			
	September 30, 2018	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable (Level 3)
Restricted cash	\$ 123,376	\$ 123,376	\$ —	\$ —

  

Description	Fair Value Measurement Using:			
	December 31, 2017	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable (Level 3)
Restricted cash	\$ 123,376	\$ 123,376	\$ —	\$ —
Warrants	\$2,679,633	\$ —	\$ —	\$2,679,633

The table below represents a rollforward of the assets and liabilities that are required to be measured at fair value on a recurring basis from December 31, 2017 to September 30, 2018:

	Significant Unobservable Inputs (Level 3)
Balance as of December 31, 2017	\$ 2,679,633
Change in fair value of warrants	1,514,775
Exercise of warrants	(4,194,408)
Balance as of September 30, 2018	\$ —

The warrants were classified as liabilities because the underlying Convertible Preferred C Shares (the "Preferred Shares") had a redemption feature in the event of a change of control of the Company. On June 5, 2018, the warrants were exercised at which time the warrant liability was determined to be \$4,194,408, which represented the difference in the market value of the Preferred Shares and the exercise price of the warrants. This resulted in an increase of the warrant liability in the amount of \$1,514,775 for the nine-month period ended September 30, 2018. The related warrant liability of \$4,194,408 was reclassified as Capital in Excess of Nominal Value at such time.

The fair values of the warrants at June 4, 2018, March 31, 2018 and December 31, 2017 were estimated using the Black-Scholes valuation model with the following assumptions:

	June 4, 2018	March 31, 2018	December 31, 2017
Risk-free interest rate	1.77%	1.86%	1.72%
Expected volatility	80%	80%	80%
Expected dividend yield	0	0	0
Expected life	1 day	5.5 months	9 months

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For the unobservable inputs for the warrants, the expected volatility was determined at each measurement date by taking an average of the volatility of other publicly-traded peer biotechnology companies. The expected life was determined at each measurement date based upon the Company's estimate of the time until the Company has a conversion event.

The fair value of the Preferred Shares was based upon recent issuances of the Company's Preferred Shares on or about December 31, 2017, March 31, 2018 and June 5, 2018.

### ***Net Loss per Ordinary Share***

Basic net loss per Ordinary Share is computed by dividing net loss by the weighted average number of shares of the Company's Ordinary Shares assumed to be outstanding during the period of computation. Diluted net loss per ordinary share is computed similar to basic net loss per share except that the denominator is increased to include the number of additional Ordinary Shares that would have been outstanding if the potential Ordinary Shares had been issued at the beginning of the year and if the additional Ordinary Shares were dilutive (treasury stock method) or the two-class method, whichever is more dilutive. For all periods presented, basic and diluted net loss per Ordinary Share are the same, as any additional Ordinary Share equivalents would be anti-dilutive.

### ***Asset Retirement Obligation***

Accounting for Asset Retirement Obligations requires legal obligations associated with the retirement of long-lived assets to be recognized at fair value when incurred and capitalized as part of the related long-lived asset. In the absence of quoted market prices, the Company estimates the fair value of its asset retirement obligations using Level 3 present value techniques, in which estimates of future cash flows associated with retirement activities are discounted using a credit-adjusted risk-free rate. Asset retirement obligations currently reported as other liabilities on the Condensed Consolidated Balance Sheet were measured during a period of historically low interest rates. The impact on measurements of new asset retirement obligations using different rates in the future may be significant.

The Company uses estimates to determine the amount of the asset retirement obligations at the end of the lease term and discounts such asset retirement obligations using an estimated discount rate. Interest on the discounted asset retirement obligation is amortized over the term of the lease using the effective interest method and is recorded as interest expense in the condensed consolidated statements of operations and comprehensive loss.

The change in asset retirement obligations is as follows:

	September 30, 2018	December 31, 2017
Balance at beginning of period	\$ 178,419	\$ 221,254
Amortization of interest	10,918	19,313
Change in estimate	—	(75,011)
Effects of exchange rate	(7,822)	12,863
Balance at end of period	<u>\$ 181,515</u>	<u>\$ 178,419</u>

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

Research and development costs are charged to expense as incurred. These costs include, but are not limited to, employee-related expenses, including salaries, benefits and travel of the Company's research and development personnel; expenses incurred under agreements with contract research organizations and investigative sites that conduct clinical and preclinical studies and manufacture the drug product for the clinical studies and preclinical activities; acquisition of in-process research and development; facilities; supplies; rent, insurance, certain legal fees, stock-based compensation, depreciation and other costs associated with clinical and preclinical activities and regulatory operations. Refundable research and development tax credits received are recorded as an offset to these costs.

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Costs for certain development activities, such as Company funded outside research programs, are recognized based on an evaluation of the progress to completion of specific tasks with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the condensed financial statements as prepaid expenses or accrued expenses, as the case may be.

### **Segment Information**

Management has concluded it has a single reporting segment for purposes of reporting financial condition and results of operations.

The following table summarizes non-current assets by geographical area:

	<u>September 30, 2018</u>	<u>December 31, 2017</u>
United States	\$ 468,922	\$ 436,463
United Kingdom	13,460,292	13,942,642
	<u>\$ 13,929,214</u>	<u>\$ 14,379,105</u>

### **Recent Accounting Pronouncements**

In June 2018, the FASB issued ASU 2018-07, *Compensation – Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*, which simplifies the accounting for share-based payments granted to nonemployees for goods and services. The ASU supersedes ASC 505-50 and expands the scope of ASC 718 to include all share-based payment arrangements related to the acquisition of goods and services from both nonemployees and employees. As a result, most of the guidance in ASC 718 associated with employee share-based payments, including most of its requirements related to classification and measurement, applies to nonemployee share-based payment arrangements. ASU 2018-07 generally requires an entity to use a modified retrospective transition approach, with a cumulative-effect adjustment to retained earnings as of the beginning of the period of adoption, for all (1) liability-classified nonemployee awards that have not been settled as of the adoption date and (2) equity-classified nonemployee awards for which a measurement date has not been established. The guidance is applicable to public business entities for fiscal years beginning after December 15, 2019 and interim periods within those years. Early adoption is permitted, and the Company adopted ASU No. 2018-07 on July 1, 2018, which did not have a material effect on the condensed consolidated financial statements.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations (Topic 805), Clarifying the Definition of a Business*, or ASU 2017-01, that clarifies the definition of a business to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. ASU 2017-01 requires an entity to evaluate if substantially all of the fair value of the gross assets acquired or disposed of is concentrated in a single identifiable asset or a group of similar identifiable assets; if so, the set of transferred assets and activities is not a business. ASU 2017-01 also requires a business to include at least an input and one substantive process that together significantly contribute to the ability to create output and removes the evaluation of whether a market participant could replace missing elements. ASU 2017-01 should be applied prospectively and is effective for annual periods beginning after December 15, 2017 and interim periods within those annual periods. The adoption of ASU 2017-01 on January 1, 2018 did not have a material effect on the Company's financial position, results of operations or cash flows.

In December 2016, the FASB issued ASU No. 2016-20, *Technical Corrections and Improvements to Topic 606, Revenue from Contracts with Customers*, or ASU 2016-20, that allows entities not to disclose variable consideration allocated to performance obligations related to either: (1) sales—or usage -based royalties on licenses of intellectual property or (2) variable consideration allocated entirely to a wholly unsatisfied performance obligation or to a wholly unsatisfied promise to transfer a distinct good or service that forms part of a single performance obligation when certain criteria are met. ASU 2016-20 also requires entities that use any of the new or previously existing optional exemptions to expand their qualitative disclosures. It also makes 12 additional technical corrections and improvements to the new revenue standard, ASU 2014-09. The amendments have the same effective date and transition requirements as ASU 2014-09. The adoption of ASU 2016-20 did not have a material effect on its financial position, results of operations or cash flows.

In November 2016, the Financial Accounting Standards Board, or FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230), Restricted Cash* (a consensus of the Emerging Issues Task Force), or ASU 2016-18, which changes the presentation of the cash flow statement to include amounts generally described as restricted cash or restricted cash equivalents, together with cash and cash equivalents, when reconciling the beginning-of-period and end-of-period amounts shown on the statement of cash flows. ASU 2016-18 also requires additional disclosures concerning the nature of the restrictions on cash and cash equivalents and a reconciliation between amounts of cash, cash equivalents and restricted cash on the balance sheet and statement of cash flows for each period presented. ASU 2016-18 will be applied retrospectively to all periods presented and is effective for public business entities for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Early adoption

is permitted, including adoption in an interim period. Prior to adoption, the Company presented changes in restricted cash as an operating activity in the statement of cash flows. Upon adoption of ASU 2016-18 on January 1, 2018, such changes are now reflected in the beginning and ending balances of cash, cash equivalents and restricted cash for all periods presented.

In October 2016, the FASB issued ASU 2016-16, *Income Taxes (Topic 740): Intra-Entity Transfers of Assets Other than Inventory*, or ASU 2016-16 which requires that an entity recognize the income tax consequences of an intra-entity transfer of assets other than inventory when the transfer occurs. The guidance must be applied using the modified retrospective basis. The Company does not expect the provisions of ASU 2016-16 to have a material impact on its current financial statements. This update will be effective for the Company at the beginning of fiscal 2019.

In May 2016, the FASB issued ASU No. 2016-12, *Revenue from Contracts with Customers (Topic 606), Narrow-Scope Improvements and Practical Expedients*, or ASU 2016-12, which amends guidance in the new revenue standard, ASU No. 2014-09 *Revenue from Contracts with Customers (Topic 606)*, or ASU 2014-09, on collectability, noncash consideration, presentation of sales tax and transition. The amendments in ASU 2016-12 are effective for annual reporting periods beginning after December 15, 2017 (i.e., January 1, 2018), including interim periods within those reporting periods, which is the same as for ASU 2014-09, as amended by ASU No. 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, or ASU 2015-14. In April 2016, the FASB issued ASU No. 2016-10, *Revenue from Contracts with Customers (Topic 606), Identifying Performance Obligations and Licensing*, or ASU 2016-10, which clarifies the principle for determining whether a good or service is “separately identifiable” from other promises in the contract and, therefore, should be accounted for as a separate performance obligation. In that regard, ASU 2016-10 requires that an entity determine whether its promise is to transfer individual goods or services to the customer, or a combined item (or items) to which the individual goods and services are inputs. In addition, ASU 2016-10 categorizes intellectual property, or IP, into two categories: “functional” and “symbolic.” Functional IP has significant standalone functionality. All other IP is considered symbolic IP. Revenue from licenses of functional IP is generally recognized at a point in time, while revenue from licenses of symbolic IP is recognized over time. ASU 2016-10 has the same effective date and transition requirements as ASU 2014-09, as amended by ASU 2015-14. In March 2016, the FASB issued ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606), Principal versus Agent Considerations (Reporting Revenue Gross versus Net)*, or ASU 2016-08, which clarifies the implementation guidance on principal versus agent considerations contained in ASU 2014-09 by specifying that the determination as to whether an entity that is involved in providing a good or a service to a customer is a principal or an agent is based upon whether the entity controls the good or the service before it is transferred to the customer. ASU 2016-08 has the same effective date and transition requirements as ASU 2014-09, as amended by ASU 2015-14. The adoption of these ASU’s on January 1, 2018 did not have a material effect on the Company’s financial position, results of operations or cash flows.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842)*. The FASB issued the update to require the recognition of lease assets and liabilities on the balance sheet of lessees. The standard will be effective for fiscal years beginning after December 15, 2018, including interim periods within such fiscal years. The ASU requires a modified retrospective transition method with the option to elect a package of practical expedients. Early adoption is permitted. The Company is currently evaluating the potential impact of the adoption of this standard on its consolidated results of operations, financial position and cash flows and related disclosures.

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers*, or ASU 2014-09, which provides a single, comprehensive revenue recognition model for all contracts with customers. The core principal of ASU 2014-09 is that an entity should recognize revenue when it transfers control of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. ASU 2014-09 also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. ASU 2014-09 is effective for annual periods, and interim periods within those annual periods, beginning after December 15, 2017 for public companies and December 15, 2018 for non-public companies. The Company is allowed to adopt ASU 2014-09 either (1) retrospectively to each prior reporting period presented using several practical expedients related to completed contracts and required disclosures, or (2) using a modified retrospective approach, with the cumulative effect of initially applying ASU 2014-09 recognized as an adjustment to the opening balance of retained earnings of the annual reporting period that includes the date of initial application, including disclosure of the effect of using this method of adoption on the financial statement line items. Because the Company has no contracts with customers, the adoption of ASU 2014-09 on January 1, 2018 did not have a material effect on the Company’s financial position, results of operations or cash flows.

### 3. Accrued Expenses

Accrued expenses for the periods presented are comprised of the following:

	<u>September 30, 2018</u>	<u>December 31, 2017</u>
Clinical Trial Costs	\$ 2,900,351	\$ 4,859,410
Professional Fees	983,677	231,923
Compensation and Benefits	872,406	2,386,903
Consulting	820,828	1,220,477
Rent	144,449	387,267
Other	320,579	246,964
	<u>\$ 6,042,290</u>	<u>\$ 9,332,944</u>

### 4. Share-Based Compensation

#### *2018 and 2016 Equity Incentive Plans*

The Company maintains the 2018 Incentive Award Plan and 2016 Equity Incentive Plan (together, the “Plans”), under which, the Company has granted share options to selected officers, employees and non-employee consultants. The Company’s board of directors administer the Plans. Options granted under the Plans have a maximum contractual term of ten years. Options granted to employees and consultants generally vest 25% on the first anniversary date of grant and the balance ratably over the next 36 months. Options granted to directors generally vest on the first anniversary date of grant. Upon the adoption of the 2018 Incentive Award Plan, the Company ceased issuing awards under the 2016 Equity Incentive Plan.

A summary of the Company’s share option activity related to employees, non-employee members of the board of directors and non-employee consultants as of and for the nine-month period ended September 30, 2018 is as follows:

	<u>Number of Options</u>	<u>Weighted-Average Exercise Price</u>	<u>Aggregate Intrinsic Value</u>
Outstanding at December 31, 2017	938,637	\$ 5.12	\$ 1,420,650
Granted	695,685	5.79	
Exercised	—	—	
Expired	—	—	
Forfeited	(4,635)	(4.98)	
Outstanding at September 30, 2018	<u>1,629,687</u>	<u>\$ 5.42</u>	<u>\$13,336,764</u>
Weighted average remaining contractual life of options outstanding as of December 31, 2017 (yrs)	<u>9.09</u>		
Weighted average remaining contractual life of options outstanding as of September 30, 2018 (yrs)	<u>8.74</u>		
Options exercisable at December 31, 2017	<u>186,395</u>	<u>\$ 7.72</u>	<u>\$ —</u>
Options exercisable at September 30, 2018	<u>411,140</u>	<u>\$ 6.43</u>	<u>\$ 2,948,369</u>
Weighted average remaining contractual life of options exercisable as of December 31, 2017 (yrs)	<u>8.21</u>		
Weighted average remaining contractual life of options exercisable as of September 30, 2018 (yrs)	<u>7.95</u>		

The total fair value of options vested during the three-month periods ended September 30, 2018 and 2017 was \$503,828 and \$41,309, respectively.

The total fair value of options vested during the nine-month periods ended September 30, 2018 and 2017 was \$1,060,177 and \$800,599, respectively.

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During the nine-month periods ended September 30, 2018 and 2017, the Company granted 695,685 and 610,645 share options. The grant date fair values of the share options granted were estimated using the Black-Scholes option valuation model with the following ranges of assumptions:

	<u>2018</u>	<u>2017</u>
Risk-free interest rate	2.32% - 2.93%	2.28% - 2.51%
Expected volatility	90%	80%
Expected dividend yield	0%	0%
Expected life (in years)	5.5 - 10.0	5.5 - 10.0

As of September 30, 2018, the total compensation expense relating to unvested options granted that had not yet been recognized was \$6,407,369, which is expected to be realized over a period of 3.96 years. The Company will issue shares upon exercise of options from Ordinary Shares reserved.

The weighted average grant date fair value of options granted during the nine-month periods ended September 30, 2018 and 2017 was \$4.46 and \$2.79, respectively.

### **Restricted Ordinary Shares**

In 2015, in connection with certain service and consulting agreements, certain employees and a consultant were awarded an aggregate of 867,935 restricted Ordinary Shares of the Company. Such shares were subject to forfeiture over a three-year service period. The shares granted to the consultant and employees were valued at \$7.72 and \$7.76 per share, respectively, and were included in loss from operations over the requisite service period. As of September 30, 2018, all such shares are no longer subject to forfeiture as the three-year service period has been completed.

On June 7, 2018, 1,306,348 restricted Ordinary Shares, which represented 5% of the fully-diluted outstanding shares of the Company as of such date, were issued to certain members of senior management in accordance with their employment agreements. One-third of such shares vested immediately, with the balance vesting quarterly over the next eight quarters beginning three months after the effectiveness of the Company's registration statement on Form S-1 filed with the SEC on June 7, 2018 (the "Registration Statement"). The shares were valued at \$15.00 per share and the related share-based compensation expense, which is recognized over the requisite service period, is included in general and administrative expenses in the condensed consolidated statements of operations. Additionally, under the terms of the employment agreements, the Company was required to pay the income taxes incurred by the grantees in connection with the grant of those restricted shares. Total compensation expense in connection with the issuance of those restricted Ordinary Shares, in the amount of \$3,405,274, of which \$1,992,182 was share-based, was recorded as general and administrative expense during the three-month period ended September 30, 2018. Total compensation expense in connection with the issuance of those restricted Ordinary Shares, in the amount of \$17,026,140, of which \$8,523,932 was share-based, was recorded as general and administrative expense during the nine-month period ended September 30, 2018.

A summary of the restricted Ordinary Shares is as follows:

	<u>Ordinary Shares</u>	<u>\$ Value</u>
Non-vested at December 31, 2017	105,913	\$ 865,861
Issued during the nine-month period ended September 30, 2018	1,306,348	19,595,220
Vesting during the nine-month period ended September 30, 2018	<u>(650,225)</u>	<u>(9,030,541)</u>
Non-vested at September 30, 2018	<u>762,036</u>	<u>\$11,430,540</u>

### **Ordinary Shares**

On March 1, 2018, a funding milestone was met under the employment agreements for certain members of senior management. Accordingly, the employees were issued an aggregate of 550,162 fully vested Ordinary Shares, which represented 3% of the fully-diluted outstanding shares of the Company as of such date. The shares were recorded as share-based compensation in the amount of \$3,096,104. Additionally, under the terms of the employment agreements, the Company was required to pay the income taxes incurred by the grantees in connection with the grant of those shares. Total compensation expense in connection with the issuance of those Ordinary Shares, in the amount of \$6,456,215, of which \$3,096,104 was share-based, was recorded as general and administrative expense during the nine-month period ended September 30, 2018.

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During the three-month and nine-month periods ended September 30, 2018 and 2017 the Company recognized total share-based compensation expense in the accompanying condensed consolidated statements of operations and comprehensive loss as follows:

	Three-month periods ended September 30,	
	2018	2017
Research and development	\$ 1,040,499	\$ 373,570
General and administrative	1,881,858	135,263
Total share based compensation	<u>\$ 2,922,357</u>	<u>\$ 508,833</u>

  

	Nine-month periods ended September 30,	
	2018	2017
Research and development	\$ 2,931,010	\$ 1,613,493
General and administrative	12,624,903	430,430
Total share based compensation	<u>\$ 15,555,913</u>	<u>\$ 2,043,923</u>

The Company does not expect to realize any tax benefits from its share option activity or the recognition of share-based compensation expense because the Company currently has net operating losses and has a full valuation allowance against its deferred tax assets. Accordingly, no amounts related to excess tax benefits have been reported in cash flows from operations or cash flows from financing activities for the three-month and nine-month periods ended September 30, 2018 and 2017.

## 5. Ordinary Shares and Convertible Preferred C Shares:

### *Ordinary Shares*

As discussed in Note 4, on March 1, 2018, a funding milestone was met under the employment agreements for certain members of senior management. Accordingly, the employees were issued an aggregate of 550,162 fully vested Ordinary Shares.

In connection with the Company's initial public offering, on June 7, 2018, the Company issued 5,000,000 Ordinary Shares at an offering price of \$15.00 per share for gross proceeds of \$75,000,000, excluding offering costs of \$9,675,735.

Also, as discussed in Note 4, on June 7, 2018, upon the effectiveness of the Company's Registration Statement, 1,306,348 restricted Ordinary Shares, which represented 5% of the fully-diluted outstanding shares of the Company as of such date, were issued to certain members of senior management in accordance with their employment agreements. One-third of such shares vested immediately, with the balance vesting quarterly over the next eight quarters.

### *Warrants*

On June 5, 2018, all of the outstanding warrants to purchase 927,594 Preferred Shares at an exercise price of approximately \$10.48 per share were exercised for aggregate cash proceeds of \$9,720,000.

### *Convertible Preferred C Shares*

During the nine-month period ended September 30, 2018, the Company issued 5,425,124 Preferred Shares at an offering price of approximately \$10.48 per share for gross proceeds of \$56,849,592, excluding offering costs of \$690,473.

Also, during the nine-month period ended September 30, 2018, the Company issued 129,419 Preferred Shares in lieu of payment of accounts payable in the aggregate amount \$1,356,129 to certain vendors.

On March 15, 2018, the Company issued 13,360 Preferred Shares in connection with a license agreement.

On June 7, 2018, upon effectiveness of the Company's Registration Statement on Form S-1, all of the 11,501,432 outstanding Preferred Shares were automatically converted into 11,501,432 Ordinary Shares. In connection with the conversion of the Preferred Shares, \$664,718 of unaccredited financing costs were fully accreted.

## 6. Net Loss per Share

The Company computes net loss per share in accordance with ASC 260-10, *Earnings per Share* (see Note 2).

Basic and diluted net loss per ordinary share is computed as follows:

	Three-month periods ended September 30,	
	2018	2017
Net loss—basic and diluted	\$ (15,424,944)	\$ (8,441,054)
Accretion of Preferred Shares financing costs	—	(130,258)
Accretion of warrants	—	(61,500)
Adjusted net loss—basic and diluted	<u>\$ (15,424,944)</u>	<u>\$ (8,632,812)</u>
Weighted-average ordinary shares outstanding:		
Basic and Diluted	26,340,450	8,607,832
Net loss per share:		
Basic and Diluted	<u>\$ (0.59)</u>	<u>\$ (1.00)</u>

  

	Nine-month periods ended September 30,	
	2018	2017
Net loss—basic and diluted	\$ (61,809,129)	\$ (22,440,158)
Accretion of Preferred Shares financing costs	(761,012)	(183,420)
Accretion of warrants	(1,045,500)	(61,500)
Adjusted net loss—basic and diluted	<u>\$ (63,615,641)</u>	<u>\$ (22,685,078)</u>
Weighted-average ordinary shares outstanding:		
Basic and Diluted	16,355,849	8,536,447
Net loss per share:		
Basic and Diluted	<u>\$ (3.89)</u>	<u>\$ (2.66)</u>

The following securities are considered to be Ordinary Share equivalents, but were not included in the computation of diluted net loss per Ordinary Share because to do so would have been anti-dilutive:

	September 30, 2018	September 30, 2017
Preferred Shares	—	2,339,578
A restricted ordinary shares subject to forfeiture	762,036	175,913
Stock options	<u>1,629,687</u>	<u>938,637</u>
	<u>2,391,723</u>	<u>3,454,128</u>

## 7. Income Taxes

The Company did not record a provision for income taxes for the three-months and nine-months ended September 30, 2018 and 2017, as the Company has generated losses for all periods.

The Company periodically evaluates the realizability of its net deferred tax assets based on all available evidence, both positive and negative. The realization of net deferred tax assets is dependent on the Company's ability to generate sufficient future taxable income during periods prior to the expiration of tax attributes to fully utilize these assets. The Company weighed both positive and negative evidence and determined that there is a continued need for a full valuation allowance on its deferred tax assets in the United States and United Kingdom as of September 30, 2018. Should the Company determine that it would be able to realize its remaining deferred tax assets in the foreseeable future, an adjustment to its remaining deferred tax assets would cause a material increase to income in the period such determination is made.

## 8. Related Party Transactions:

### *Transition Services Agreement*

Effective April 24, 2015, the Company entered into a three-year transition services agreement (the "TSA") with Kadmon, which is a minority shareholder of the Company, whereby Kadmon would provide office and laboratory facilities as well as certain other personnel support activities to the Company. Under the agreement, the Company was charged for (i) rent based upon the square footage of the office and laboratory facilities used by the Company (ii) other personnel support activities based upon the hours of the personnel providing the support activities, and (iii) and other direct costs incurred by Kadmon on behalf of the Company, plus a 7% administrative fee. The TSA terminated on April 24, 2018 and the Company is currently leasing office space on a month to month basis from Kadmon.

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During the three-month periods ended September 30, 2018 and 2017, the Company incurred the following charges from Kadmon, which are included in loss from operations:

	2018	2017
Rent	\$140,805	\$136,353
Personnel	—	5,202
Other	—	41
Total charges incurred	<u>\$140,805</u>	<u>\$141,596</u>

During the nine-month periods ended September 30, 2018 and 2017, the Company incurred the following charges from Kadmon, which are included in loss from operations:

	2018	2017
Rent	\$416,479	\$411,877
Personnel	6,493	30,480
Other	—	5,247
Total charges incurred	<u>\$422,972</u>	<u>\$447,604</u>

During the three-month periods ended September 30, 2018 and 2017, the Company made cash payments totaling \$140,954 and \$0, respectively, to Kadmon.

During the nine-month periods ended September 30, 2018 and 2017, the Company made cash payments totaling \$1,284,258 and \$275,941, respectively, to Kadmon.

The amount due to Kadmon at September 30, 2018 and December 31, 2017 is \$0 and \$861,030, respectively and is disclosed as Due to Kadmon on the Company's condensed consolidated balance sheets.

### **Research Agreement**

Effective October 23, 2016, the Company entered into a four-year master services agreement with UCL Consultants Limited, an entity affiliated with University College of London ("UCL"), which is a shareholder of the Company. Pursuant to the agreement, UCL Consultants Limited provides pre-clinical research and development under the direction of the Company. In connection with the agreement, the Company issued several work orders during the year ended December 31, 2017 in the aggregate amount of £241,053, or approximately \$311,000, based upon the average exchange rate during the year ended December 31, 2017. Either party may terminate the agreement by giving 30 days written notice.

Total research and development expenses under this agreement for the three-month periods ended September 30, 2018 and 2017 were approximately \$137,000 and \$112,000, respectively.

Total research and development expenses under this agreement for the nine-month periods ended September 30, 2018 and 2017 was approximately \$509,000 and \$334,000, respectively.

Future obligations, under the agreement equal £695,321, or approximately \$905,934, through October 2020.

The amount due to UCL under the master services agreement at September 30, 2018 and December 31, 2017 is \$484,408 and \$775,315, respectively, and is included in accounts payable and accrued expenses on the condensed consolidated balance sheets.

### **Manufacturing Agreement**

Effective September 1, 2016, the Company entered into a manufacturing and drug supply agreement with UCL. Pursuant to the agreement, UCL manufactured materials for the Company's clinical trials under the direction of the Company. Either party could terminate the agreement by giving 30 days written notice. The agreement was terminated in January 2018.

Total research and development expenses under this agreement for the three-month periods ended September 30, 2018 and 2017 was approximately \$0 and \$567,150, respectively.

Total research and development expenses under this agreement for the nine-month periods ended September 30, 2018 and 2017 was approximately \$0 and \$1,609,668, respectively.

The amount due to UCL under the manufacturing and drug supply agreement at September 30, 2018 and December 31, 2017 is \$0 and \$2,466,142, respectively, and is included in accrued expenses in the condensed consolidated balance sheet.

### ***License Agreement***

Effective March 15, 2018, the Company entered into an exclusive worldwide license agreement with UCL Business, PLC (“UCL Business”), to develop up to eight programs using certain ocular gene therapy technology. Under the terms of the agreement, the Company has agreed to pay UCL Business certain sales milestone payments, if achieved, in the aggregate amount of £39.8 million, or approximately \$51.9 million using the exchange rate at September 30, 2018, and royalties on net sales, as defined upon commercialization. Additionally, the Company is responsible for all patent prosecution and maintenance costs incurred and has also agreed to pay UCL Business an annual maintenance fee of £50,000, or approximately \$66,000, until the first commercial sale of a product. The agreement will terminate upon the later of (i) the last valid claim in a relevant product, (ii) the expiration of regulatory exclusivity to all licensed products, or (iii) the 10<sup>th</sup> anniversary of the first commercial sale of a product.

The Company did not incur any research and development expenses under the agreement during the three-month and nine-month periods ended September 30, 2018 and 2017.

### ***Leases***

#### ***December 2016 Lease***

Effective December 15, 2016, the Company entered into a non-cancellable operating lease with ARE, expiring on October 31, 2032, for laboratory and office facilities in New York. ARE is an entity that is under common control by an entity that is a minority shareholder of the Company and whose CEO is a director of the Company. The lease provided for monthly base rent, including rent escalations, property management fees and rent holidays, plus operating expenses during the lease term. The Company recorded monthly rent expense on a straight-line basis from December 15, 2016 through October 31, 2032. On October 26, 2017, the lease was amended, whereby the lease would terminate on March 31, 2018 and only base rent and management fees in the aggregate amount of \$563,507 would be due from November 1, 2017 through March 31, 2018. Under the amendment, the Company issued a note to ARE in the amount of \$1,442,009, removed the balance of the deferred rent and accrued the future rent payments, all of which were recorded as rent expense at the time of the amendment, in accordance with ASC 420, Exit and Disposal Activities, as the Company had a cease use date as of the date of the amendment. The balance of deferred lease obligation, representing the difference between cash rent paid and straight-line rent expense, was \$0 as of December 31, 2017 and September 30, 2018.

Total rent expense under this operating lease was \$0 and \$390,903 for the three-month periods ended September 30, 2018 and 2017, respectively.

Total rent expense under this operating lease was \$0 and \$1,172,709 for the nine-month periods ended September 30, 2018 and 2017, respectively.

On October 26, 2017, in connection with the amendment to the lease, the Company issued a promissory note in the amount of \$1,442,009 to ARE. The note accrued interest at the rate of 5% per annum and was due on December 31, 2018. However, if the Company had sufficient liquidity, as defined in the note, then the note, including accrued interest, would become due and payable at that time. In accordance with the sufficient liquidity provision, the Company repaid the note, plus accrued interest, in the aggregate amount of \$1,472,433 during the three-month period ended March 31, 2018.

The Company recorded interest expense of \$0 and \$30,424 for the three-month and nine-month periods ended September 30, 2018.

#### ***July 2016 Lease***

Effective July 1, 2016, the Company entered into a non-cancellable operating lease for laboratory and related office facilities in New York with ARE. The lease provides for monthly base rent and property management fees, including rent escalations and rent holidays, plus operating expenses during the lease term, which expires on December 31, 2021. The Company records monthly rent expense on a straight-line basis from July 1, 2016 through December 31, 2021. As of September 30, 2018 and December 31, 2017, the balance of deferred rent, representing the difference between cash rent paid and straight-line rent expense, was \$210,993 and \$231,276, respectively.

Total rent expense under this operating lease was \$121,888 and \$121,889 for the three-month periods ended September 30, 2018 and 2017, respectively.

Total rent expense under this operating lease was \$365,668 and \$365,669 for the nine-month periods ended September 30, 2018 and 2017, respectively.

As of September 30, 2018, the aggregate future minimum rental payments under this lease are \$1,795,570.

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In connection with the signing of this lease, the Company entered into a standby letter of credit agreement for \$122,866, which serves as a security deposit for the premises. The standby letter of credit expires on July 7, 2017 and is automatically renewed annually through July 7, 2021. This standby letter of credit is secured with restricted cash in a money market account.

The aggregate future minimum rental payments under this lease are as follow:

2018	\$ 131,618
2019	535,683
2020	554,432
2021	573,837
Total future rent payments	<u>\$1,795,570</u>

### 9. Commitments:

On September 7, 2018, the Company entered into an exclusive licensing agreement with the National Institutes of Health (“NIH”) for worldwide rights to expanded indications for use of AAV-AQP1 for treatment of xerostomia (dry mouth) and xerophthalmia (dry eye) associated with Sjögren’s syndrome. This agreement expands the Company’s original exclusive licensing agreement with the NIH for exclusive worldwide rights to AAV-AQP1 that was executed as of November 9, 2017. AAV-AQP1 is currently in Phase 1/2 development for treatment of grade 2 or 3 radiation-induced xerostomia.

On July 27, 2018 two leases for office and laboratory facilities in London, UK expired. Effective July 27, 2018, the Company entered into two new non-cancellable operating leases for the same office and laboratory facilities in London. The leases provide for annual base rent in the aggregate amount of approximately \$363,000, plus operating expenses, through May 31, 2022, at which time the annual base rent will be revalued based on market rates at that time. The leases expire on May 24, 2027.

The aggregate future minimum rental payments under these leases are as follow:

2018	\$ 89,565
2019	358,258
2020	358,258
2021	358,258
2022	358,258
Thereafter	1,582,308
Total future rent payments	<u>\$3,104,905</u>

### 10. Subsequent Events:

Management has evaluated subsequent events through the date of this filing. Based on our evaluation, the following disclosures have been made:

On October 5, 2018, the Company entered into an agreement to acquire Vector Neurosciences Inc. (“Vector”) pursuant to an Agreement and Plan of Merger (the “Merger Agreement”) by and among the Company, Vector, VN Acquisition, Inc., a wholly-owned subsidiary of the Company (“Merger Sub 1”), VN Acquisition 2, Inc., a wholly-owned subsidiary of the Company (“Merger Sub 2”), the Vector stockholders named therein and the Vector stockholder representative, pursuant to which Merger Sub 1 was merged with and into Vector, with Vector being the surviving corporation (“Merger 1”) and, immediately following Merger 1, Vector was merged with and into Merger Sub 2, with Merger Sub 2 being the surviving corporation (together with Merger 1, the “Merger”). As a result of the Merger, Vector is a wholly-owned subsidiary of the Company. The Company’s board of directors, Vector’s board of directors and Vector’s stockholders have, in each case, unanimously approved the Merger, the Merger Agreement and the transactions contemplated by the Merger Agreement. The merger consideration to Vector’s stockholders consists of 225,000 shares of the Company’s Ordinary Shares as initial merger consideration, consisting of 202,500 shares which were issued at the closing of the Merger and an additional 22,500 shares to be issued 18 months following the closing, subject to any indemnification claims under the Merger Agreement. Based on the closing price of the Company’s Ordinary Shares on October 5, 2018, the value of the initial merger consideration is approximately \$3.0 million. In addition, pursuant to the terms of the Merger Agreement, the Company will issue to Vector’s stockholders additional Ordinary Shares equal to a maximum value of \$21 million if specified regulatory milestones are met and will make royalty payment to Vector’s stockholders in an amount equal to a percentage of the value of sales of certain products developed based on the Vector assets, which royalty payments are also payable in Ordinary Shares. The number of Ordinary Shares to be issued in connection with such milestones and royalties will be

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based on the three-day average closing price of the Company's Ordinary Shares immediately prior to the date of determination of the value of the payment. As a result of the acquisition, the Company has expanded its portfolio of clinical stage product candidates to include adeno-associated virus encoding glutamic acid decarboxylase (AAV-GAD), a gene therapy product candidate ready for continued Phase 2 clinical development for Parkinson's disease. A prior Phase 2 clinical trial of AAV-GAD was completed and was the first successful randomized, double-blind, sham-controlled trial of its kind for a gene therapy product candidate targeting a brain disorder.

On October 9, 2018, the Company entered into a research collaboration agreement with Janssen Pharmaceuticals, Inc. ("Janssen"), one of the Janssen Pharmaceutical Companies of Johnson & Johnson, to develop regulatable gene therapy treatment using the Company's proprietary riboswitch technology. As part of the agreement, the Company will use its proprietary riboswitch technology to engineer regulatable gene therapy constructs encoding proprietary gene sequences from Janssen.

## **Item 2. Management’s Discussion and Analysis of Financial Condition and Results of Operations.**

*You should read the following discussion and analysis of financial condition and operating results together with our financial statements and related notes appearing in this Quarterly Report on Form 10-Q and those included in our final prospectus that forms a part of the Company’s registration statement on Form S-1 (Reg. No. 333-224914), filed with the Securities and Exchange Commission (“SEC”) pursuant to Rule 424(b)(4) on June 8, 2018 (the “Prospectus”). Some of the information contained in this discussion and analysis or set forth elsewhere in the Quarterly Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many important factors, including those set forth in the “Risk Factors” section of this Quarterly Report on Form 10-Q, our actual results could differ materially from the results described in, or implied by, the forward-looking statements contained in the following discussion and analysis. For convenience of presentation some of the numbers have been rounded in the text below. Unless the context requires otherwise, references in this Management’s Discussion and Analysis of Financial Condition and Results of Operations to the “Company,” “we,” “us” and “our” refer to (i) MeiraGTx Limited and its subsidiaries prior to the Reorganization Transactions and (ii) MeiraGTx Holdings plc and its subsidiaries upon completion of the Reorganization Transactions, as applicable.*

### **Overview**

We are a vertically integrated, clinical stage gene therapy company with four ongoing clinical programs and a broad pipeline of preclinical and research programs. We have core capabilities in viral vector design and optimization, gene therapy manufacturing as well as a potentially transformative gene regulation technology. We have taken a portfolio approach by licensing, acquiring and developing technologies that give us depth across both product candidates and indications. Though initially focusing on the eye, salivary gland and central nervous system, we intend to expand our focus in the future to develop additional gene therapy treatments for patients suffering from a range of serious diseases.

We are an exempted company incorporated under the laws of the Cayman Islands in 2018, and prior to that, we commenced operations as MeiraGTx Limited, a private limited company incorporated under the laws of England and Wales in 2015. Our discussion of our financial condition and results of operations is based upon our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. Since our formation, we have devoted substantially all of our resources to developing our technology platform, establishing our viral vector manufacturing facility and developing manufacturing processes, advancing the product candidates in our ophthalmology, salivary gland and neurodegenerative disease programs, building our intellectual property portfolio, organizing and staffing our company, business planning, raising capital, and providing general and administrative support for these operations. In 2016, we completed the acquisition of assets held by BRI-Alzan, Inc., a Delaware corporation, including a worldwide license agreement to develop certain preclinical technology for the treatment of ALS. In October 2018, we completed the acquisition of Vector Neurosciences, Inc., a Delaware Corporation including the AAV-GAD gene therapy program which had completed a randomized, sham-controlled Phase 2 study for treatment of Parkinson’s disease. To date, we have financed our operations primarily with cash on hand and proceeds from the sales of our Convertible Preferred C Shares (“Preferred Shares”) and ordinary shares (“Ordinary Shares”). Through September 30, 2018, we received gross proceeds of approximately \$175.6 million from sales of our Ordinary and Preferred Shares. As of September 30, 2018, we had cash and cash equivalents of \$88.6 million.

We are a clinical stage company and have not generated any product revenues to date. We have five clinical programs and a pipeline of preclinical programs. Since inception, we have incurred significant operating losses. Our net losses for the three months ended September 30, 2018 and 2017 were \$15.4 million and \$8.4 million, respectively, and for the nine months ended September 30, 2018 and 2017 were \$61.8 million and \$22.4 million, respectively. As of September 30, 2018, we had an accumulated deficit of \$127.2 million. We do not expect to generate revenue from sales of any products for several years, if at all.

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We expect our operating expenses to increase substantially in connection with our ongoing development activities related to our product candidates. We anticipate that our expenses will increase due to costs associated with our clinical development program targeting in achromatopsia due to mutations in the *CNGB3* or *CNGA3* gene, inherited retinal dystrophy caused by mutations in *RPE65*, or *RPE65*-deficiency, and X-Linked retinitis pigmentosa, or XLRP. In addition, we expect to incur increasing costs associated with our clinical activities for *hAQP1* for the treatment of radiation-induced xerostomia and xerostomia (dry mouth) and xerophthalmia (dry eye) associated with *Sjögren's* syndrome. We are currently evaluating potential next steps for clinical development of AAV-GAD, which remains pending future discussions with regulatory agencies. We also expect to incur expenses related to research activities in additional therapeutic areas to expand our pipeline, hiring additional personnel in manufacturing, research, clinical trials, quality and other functional areas, and associated cash and share-based compensation expense, as well as the further development of internal manufacturing capabilities and capacity and other associated costs including the management of our intellectual property portfolio.

As a result of these anticipated expenditures, we will require additional capital, which we may raise through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources to enable us to complete the development and potential commercialization of our product candidates. Furthermore, we expect to incur additional costs associated with being a public company. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our product candidate development efforts. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate certain of our research and development programs.

Based on our current cash and cash equivalents, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2020. We have based these estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. See “—Liquidity and Capital Resources.” Because of the numerous risks and uncertainties associated with the development of our product candidates, any future product candidates, our platform and technology and because the extent to which we may enter into collaborations with third parties for development of any of our product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements will depend on many factors, including:

- the initiation, progress, timing, costs and results of our planned clinical trials for our product candidates;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, EMA and other regulatory authorities;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or any of our product candidates;
- the effect of competing technological and market developments;
- the costs and timing of further developing our manufacturing facilities in the United Kingdom;
- the costs of operating as a public company;
- the extent to which we in-license or acquire other products and technologies;
- the cost of establishing sales, marketing and distribution capabilities for our product candidates in regions where we choose to commercialize our products; and
- the initiation, progress, timing and results of our commercialization of our product candidates, if approved for commercial sale.

Adequate additional funds may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. Any future debt financing or preferred equity or other financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute your ownership interests.

If we raise additional funds through collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs 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 or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

### **Clinical Development Highlights**

**AAV-CNGB3:** Treated two additional pediatric patients in the extension phase of the Phase 1/2 study, bringing the total number of patients treated to sixteen (eleven adults and five pediatrics). We anticipate completing dosing of the pediatric extension phase in 2018.

**AAV-RPGR:** Completed dose escalation phase of the Phase 1/2 study, bringing the total number treated to ten patients. We expect to initiate dosing in the pediatric extension phase of the study in 2018.

**AAV-RPE65:** Dosing in the Phase 1/2 clinical study was completed in the second quarter of 2018. A total of nine adults were treated in three escalating dose cohorts. Six pediatric patients were treated in the pediatric extension arm of the study.

**AAV-CNGA3:** cGMP manufacturing of clinical material is ongoing in our manufacturing facility. We anticipate release in the next few months with the initiation of the treatment study in early 2019.

**Natural History Studies:** We continue to enroll patients in the achromatopsia, XLRP and RPE65 long-term natural history studies in Europe and the US, and our long-term follow-up studies in each indication.

### **Regulatory Highlights**

**Received Orphan Drug Designation from FDA for Achromatopsia Treatment (AAV-CNGA3):** On August 7, 2018, the Food and Drug Administration (FDA) granted orphan drug designation for our AAV-CNGA3 gene therapy product candidate for the treatment of achromatopsia caused by mutations in the *CNGA3* gene.

**Received Fast Track Designation from FDA for Achromatopsia Treatment (AAV-CNGB3):** On August 16, 2018, the FDA granted Fast Track designation for our AAV-CNGB3 gene therapy product candidate for the treatment of achromatopsia caused by mutations in the *CNGB3* gene.

**Received Rare Pediatric Disease Designation from FDA for Achromatopsia Treatment (AAV-CNGA3):** On August 21, 2018, the Offices of Orphan Products Development and Pediatric Therapeutics of the FDA granted rare pediatric disease designation for our AAV-CNGA3 gene therapy product candidate for the treatment of achromatopsia caused by mutations in the *CNGA3* gene.

### **Corporate Highlights**

**Entered Into an Exclusive Licensing Agreement with the National Institute of Health (“NIH”):** On September 7, 2018, we entered into an exclusive licensing agreement with the National Institute of Dental and Craniofacial Research, a division of the NIH, for gene therapy treatment of *Sjögren’s* syndrome and associated xerostomia (dry mouth) or xerophthalmia (dry eye). Under the agreement, we will receive worldwide rights to adeno-associated virus vector mediated gene delivery of aquaporin-1, designed AAV-AQP1, for *Sjögren’s* syndrome patients with associated xerostomia or xerophthalmia.

**Completed Acquisition of Vector Neurosciences, Inc.:** On October 5, 2018, we acquired Vector Neurosciences Inc. (“Vector”) in an all-stock transaction. As a result of the acquisition, we have expanded our portfolio of clinical stage product candidates to include adeno-associated virus encoding glutamic acid decarboxylase (AAV-GAD), a gene therapy product candidate ready for continued Phase 2 clinical development for Parkinson’s disease. A prior Phase 2 clinical trial of AAV-GAD was completed and was the first successful randomized, double-blind, sham-controlled trial of its kind for a gene therapy product candidate targeting a brain disorder.

**Entered Into a Research Collaboration Agreement with Janssen:** On October 9, 2018, we entered into a research collaboration agreement with Janssen Pharmaceuticals, Inc., one of the Janssen Pharmaceutical Companies of Johnson & Johnson, involving our proprietary riboswitch technology in gene regulation. As part of the agreement, we will use our proprietary riboswitch technology to engineer regulatable gene therapy constructs encoding proprietary gene sequences from Janssen. Evaluation of the performance of these constructs will determine the utility of this approach in future product development.

## Components of Our Results of Operations

### Operating Expenses

Our operating expenses since inception have consisted primarily of general and administrative costs and research and development costs.

#### General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including share-based compensation, for personnel in our executive, finance, business development and administrative functions. General and administrative expenses also include legal fees relating to intellectual property and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and office facility-related expenses, which include direct depreciation costs.

We expect that our general and administrative expenses will increase in the future as we increase our personnel headcount to support increased research and development activities. We have also incurred and expect to continue to incur increased expenses associated with being a public company, including costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with Nasdaq and SEC requirements; director and officer insurance costs; and investor and public relations costs.

#### Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our product candidates, and include:

- employee-related expenses, including salaries, benefits and travel of our research and development personnel;
- expenses incurred in connection with third-party vendors that conduct clinical and preclinical studies and manufacture the drug product for the clinical trials and preclinical activities;
- acquisition of in-process research and development;
- costs associated with clinical and preclinical activities including costs related to facilities, supplies, rent, insurance, certain legal fees, share-based compensation, and depreciation; and
- expenses incurred with the development and operation of our manufacturing facility.

We expense research and development costs as incurred.

We typically use our employee and infrastructure resources across our development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, license payments made under our licensing arrangements or other internal costs to specific development programs or product candidates. These costs are included in other research and development expenses in the table below.

The following table summarizes our research and development expenses:

	Three Months Ended			Nine Months Ended		
	2018	September 30, 2017	Change	2018	September 30, 2017	Change
Ophthalmology program	\$1,153,238	\$1,239,642	\$ (86,404)	\$ 3,922,392	\$ 3,006,618	\$ 915,774
Salivary gland program	208,763	178,622	30,141	643,998	691,110	(47,112)
Neurodegeneration program	661,872	1,088,255	(426,383)	1,723,578	2,000,592	(277,014)
Manufacturing	1,395,661	761,588	634,073	3,710,966	1,570,043	2,140,923
Other research and development costs	4,689,626	3,120,120	1,569,506	12,826,242	9,306,766	3,519,476
Total research and development expenses	<u>\$8,109,160</u>	<u>\$6,388,227</u>	<u>\$1,720,933</u>	<u>\$22,827,176</u>	<u>\$16,575,129</u>	<u>\$6,252,047</u>

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase substantially for the foreseeable future as we initiate additional preclinical and clinical trials of our existing product candidates and continue to discover and develop additional product candidates.

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We cannot determine with certainty the duration and costs of future clinical trials of our product candidates or any other product candidate we may develop or if, when, or to what extent we will generate revenue from the commercialization and sale of any product candidate for which we obtain marketing approval. We may never succeed in obtaining marketing approval for any product candidate. The duration, costs and timing of clinical trials and development of our existing product candidates or any other product candidate we may develop will depend on a variety of factors, including:

- the scope, rate of progress, expense and results of clinical trials of our existing product candidates, as well as of any future clinical trials of other product candidates and other research and development activities that we may conduct;
- uncertainties in clinical trial design and patient enrollment rates;
- the actual probability of success for our product candidates, including the safety and efficacy, early clinical data, competition, manufacturing capability and commercial viability;
- significant and changing government regulation and regulatory guidance;
- the timing and receipt of any marketing approvals; and
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

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

### ***Other non-operating income (expense)***

Other non-operating income (expense) includes the following:

#### *Foreign currency (loss) gain*

Our condensed consolidated financial statements are presented in U.S. dollars, which is our reporting currency. The financial position and results of operations of our subsidiaries MeiraGTx UK II and MeiraGTx B.V. are measured using the foreign subsidiaries' local currency as the functional currency. MeiraGTx UK II cash accounts holding U.S. dollars are remeasured based upon the exchange rate at the date of remeasurement with the resulting gain or loss included in the condensed consolidated statement of operations and comprehensive loss. Expenses of such subsidiaries have been translated into U.S. dollars at average exchange rates prevailing during the period. Assets and liabilities have been translated at the rates of exchange on the condensed consolidated balance sheet date. The resulting translation gain and loss adjustments are recorded directly as a separate component of shareholders' equity and as other comprehensive loss on the condensed consolidated statement of operations and comprehensive loss.

#### *Change in fair value of warrant liability*

We have determined that our warrants are classified as liabilities on our balance sheet because the Preferred Shares underlying the warrants have a redemption feature in the event of a change of control of the Company. The fair values of the warrants are estimated using the Black-Scholes valuation model with certain assumptions regarding risk free interest rate, expected volatility, expected dividend yield and expected life. The Black-Scholes value of the warrants was recorded as a warrant liability and is remeasured quarterly. Any changes in the quarterly valuation of the warrants is charged to operations.

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

Management's discussion and analysis of our financial condition and results of operations is based on our condensed consolidated financial statements, which have been prepared in accordance with the accounting principles generally accepted in the United States of America ("GAAP"). The preparation of these condensed consolidated financial statements requires us to make estimates and judgements that affect the reporting amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our condensed consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgements, including those related to warrant liabilities, share-based compensation and accrued expenses. We base our estimates on historical experience, known trends and events and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgements about the carrying value of assets and liabilities that are not readily apparent from our sources. Actual results may differ from these estimates under different assumptions.

**Critical accounting policies**

The Company's significant accounting policies are disclosed in the audited financial statements for the year ended December 31, 2017 included in the Company's Prospectus and Note 2 to our unaudited condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q. The Company has adopted the new accounting pronouncements which are disclosed further in Note 2 to the condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q.

**Recent Accounting Pronouncements**

See Note 2 of the notes to our unaudited condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q for a summary of recently issued and adopted accounting pronouncements.

**Results of Operations****Comparison of Three Months Ended September 30, 2018 and 2017**

The following table summarizes our results of operations for the three months ended September 30, 2018 and 2017, respectively

	Three Months Ended September 30,		
	2018	2017	Change
<b>Operating expenses:</b>			
General and administrative	\$ 6,629,052	\$ 2,374,527	\$ 4,254,525
Research and development	8,109,160	6,388,227	1,720,933
Total operating expenses	14,738,212	8,762,754	5,975,458
Loss from operations	(14,738,212)	(8,762,754)	(5,975,458)
<b>Other non-operating income (expense)</b>			
Other income	—	—	—
Foreign currency (loss) gain	(677,488)	391,521	(1,069,009)
Interest income	264	2,915	(2,651)
Interest expense	(9,508)	(72,736)	63,228
<b>Net loss</b>	<b><u>\$(15,424,944)</u></b>	<b><u>\$(8,441,054)</u></b>	<b><u>\$(6,983,890)</u></b>

**General and Administrative Expenses**

General and administrative expenses were \$6.6 million for the three months ended September 30, 2018, compared to \$2.4 million for the three months ended September 30, 2017. The increase of \$4.2 million was primarily due to increases of \$1.7 million in payroll, \$1.8 million in share-based compensation, \$0.7 million in legal and accounting fees, \$0.2 million in investor relations costs and \$0.3 million in insurance costs, which was partially offset by decreases of \$0.4 million in rent and \$0.1 million in depreciation expenses.

**Research and Development Expenses**

Research and development expenses for the three months ended September 30, 2018 were \$8.1 million, compared to \$6.4 million for the three months ended September 30, 2017. The increase of \$1.7 million was primarily due to an increase in costs of \$2.1 million related to preparation of our manufacturing facility for production, \$0.6 million in share-based compensation and \$0.2 million in legal fees, which was partially offset by a decrease of \$1.2 million in clinical trial material costs.

**Foreign Currency (Loss) Gain**

Foreign currency loss was \$0.7 million for the three months ended September 30, 2018 compared to a gain of \$0.4 million for the three months ended September 30, 2017. The increase of \$1.1 million was primarily due to a strengthening U.S. dollar against the pound sterling during the three months ended September 30, 2018.

### Comparison of Nine Months Ended September 30, 2018 and 2017

The following table summarizes our results of operations for the nine months ended September 30, 2018 and 2017, respectively

	Nine Months Ended September 30,		
	2018	2017	Change
<b>Operating expenses:</b>			
General and administrative	\$ 35,129,120	\$ 6,744,963	\$ 28,384,157
Research and development	22,827,176	16,575,129	6,252,047
Total operating expenses	57,956,296	23,320,092	34,636,204
Loss from operations	(57,956,296)	(23,320,092)	(34,636,204)
<b>Other non-operating income (expense)</b>			
Other income	83,075	—	83,075
Foreign currency (loss) gain	(2,425,488)	990,395	(3,415,883)
Change in fair value of warrant liability	(1,514,775)	—	(1,514,775)
Interest income	50,926	21,295	29,631
Interest expense	(46,571)	(131,756)	85,185
Net loss	<u><u>\$(61,809,129)</u></u>	<u><u>\$(22,440,158)</u></u>	<u><u>\$(39,368,971)</u></u>

#### General and Administrative Expenses

General and administrative expenses were \$35.1 million for the nine months ended September 30, 2018, compared to \$6.7 million for the nine months ended September 30, 2017. The increase of \$28.4 million was primarily due to increases of \$15.2 million in payroll, \$12.2 million in share-based compensation, \$0.2 million in consultant costs, \$1.0 million in legal and accounting fees, \$0.2 million in travel expenses, \$0.4 million in insurance costs, \$0.3 million in investor relations costs and \$0.3 million in other costs, which was partially offset by decreases of \$1.1 million in rent and \$0.3 million in depreciation expenses.

#### Research and Development Expenses

Research and development expenses for the nine months ended September 30, 2018 were \$22.8 million, compared to \$16.6 million for the nine months ended September 30, 2017. The increase of \$6.2 million was primarily due to an increase in costs of \$6.0 million related to preparation of our manufacturing facility for production, \$1.2 million in share-based compensation, \$0.2 million in rent, \$0.2 million in license fees, \$0.2 million in payroll and related fees, \$0.2 million in travel costs, \$0.2 million in legal fees and \$0.3 million in other costs, which was partially offset by a decrease of \$2.3 million in clinical trial material costs.

#### Foreign Currency (Loss) Gain

Foreign currency loss was \$2.4 million for the nine months ended September 30, 2018 compared to a gain of \$1.0 million for the nine months ended September 30, 2017. The increase of \$3.4 million was primarily due to a strengthening U.S. dollar against the pound sterling during the nine months ended September 30, 2018.

#### Change in Fair Value of Warrant Liability

The change in fair value of the warrant liability for the nine months ended September 30, 2018 was due to the revaluation of warrants, which were issued to certain investors in September and November 2017. On June 5, 2018, the warrants were exercised at which time the warrant liability was determined to be \$4,194,408, which represented the difference in the market value of the Preferred Shares and the exercise price of the warrants. As a result of the revaluation, there was an increase of \$1.5 million in the fair market value of the warrant liability at September 30, 2018, which resulted in a gain being recorded for the nine months ended September 30, 2018.

#### Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have not generated positive cash flows from operations, and there are no assurances that we will be successful in obtaining an adequate level of financing for the development and commercialization of our product candidates. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the preclinical and clinical development of our product candidates. We expect that our research and development and general and administrative costs will increase in connection with conducting preclinical studies and clinical trials for our product candidates, building out internal capacity to have product manufactured to support preclinical studies and clinical trials, expanding our intellectual property portfolio, and providing general and administrative support for our operations. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements, or other sources.

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We are required to maintain a stand-by letter of credit as a security deposit under a certain lease with ARE, an entity that is under common control with an entity that is a minority shareholder of the Company and whose CEO is on our board of directors. Our bank requires us to maintain restricted cash balances to serve as collateral for the letter of credit issued to the landlord by the bank. As of September 30, 2018 and December 31, 2017, the restricted cash balances for the ARE lease was invested in a commercial money market account. The restricted cash balance for the ARE lease remains at \$123,376 through the end of the lease term in December 2021, plus three months. We had \$123,376 of restricted cash included in long-term assets as of September 30, 2018 and December 31, 2017. We do not currently have any approved products and have never generated any revenue from product sales. To date, we have financed our operations primarily through the sale of our Ordinary Shares and Preferred Shares. On June 7, 2018, upon effectiveness of our registration statement on Form S-1 (File No. 333-224914), as amended, filed in connection with our IPO (the "Registration Statement"), all of the 11,501,432 outstanding Preferred Shares were automatically converted into 11,501,432 Ordinary Shares.

### **Cash Flows**

As of September 30, 2018, we had \$88.6 million of cash and cash equivalents.

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

	<b>For the nine -month periods ended September 30,</b>	
	<b>2018</b>	<b>2017</b>
Net cash used in operating activities	\$ (47,419,158)	\$ (14,345,935)
Net cash used in investing activities	(2,372,622)	(8,389,156)
Net cash provided by financing activities	130,047,495	10,214,271
Increase (decrease) in cash	<u>\$ 80,255,715</u>	<u>\$ (12,520,820)</u>

#### *Operating Activities*

During the nine months ended September 30, 2018, our cash used in operating activities of \$47.4 million was primarily due to our net loss of \$61.8 million as we incurred expenses associated with research activities on our clinical programs and research activities for our other product candidates and incurred general and administrative expenses. The loss included non-cash charges of \$21.0 million, which consisted of \$15.6 million of share-based compensation, depreciation of \$1.5 million, foreign currency loss of \$2.4 million and a change in the fair value of a warrant liability of \$1.5 million. Additionally, operating assets, consisting of prepaid expenses, security deposits and other current assets, increased by \$0.1 million and operating liabilities, consisting of accounts payable, accrued expenses and due to affiliate decreased by \$6.7 million.

During the nine months ended September 30, 2017, our cash used in operating activities of \$14.3 million was primarily due to our net loss of \$22.4 million as we incurred expenses associated with research activities on our clinical programs and research activities for our other product candidates and incurred general and administrative expenses. The loss included non-cash charges of \$1.6 million, which consisted of \$2.0 million of share-based compensation, depreciation of \$0.6 million, which was partially offset by a foreign currency gain of \$1.0 million. Additionally, operating assets, consisting of prepaid expenses and other current assets increased by \$1.2 million, and operating liabilities, consisting of accounts payable, accrued expenses, deferred rent and due to Kadmon, increased by \$7.7 million.

#### *Investing Activities*

Net cash used in investing activities for the nine months ended September 30, 2018 of \$2.4 million consisted of purchases of property and equipment, primarily for our manufacturing facility.

Net cash used in investing activities for the nine months ended September 30, 2017 of \$8.4 million consisted of purchases of property and equipment, primarily for our manufacturing facility.

### *Financing Activities*

Net cash provided by financing activities was \$130.0 million for the nine months ended September 30, 2018, which consisted of net proceeds of \$65.6 million from the issuance of Ordinary Shares in connection with our initial public offering, \$56.2 million from the issuance of Preferred Shares, \$9.7 million from the exercise of warrants, which was partially offset by the payment of a note in the amount of \$1.4 million.

Net cash provided by financing activities was \$10.2 million for the nine months ended September 30, 2017, which represented proceeds from the issuance of our Preferred Shares of \$7.7 million and the issuance of a note payable of \$2.5 million.

### *Funding Requirements*

Our operating expenses have increased substantially in 2017 and 2018 and are expected to increase substantially in the future in connection with our ongoing activities, particularly as we advance our clinical activities including scale-up of manufacturing processes and additional clinical trials. In addition, we expect to incur additional costs associated with operating as a public company.

Specifically, our expenses will increase as we:

- pursue the preclinical and clinical development of our product candidates;
- scale up our manufacturing processes and capabilities to support our preclinical studies and clinical trials of our product candidates;
- in-license or acquire the rights to other products, product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;
- hire additional personnel in research, manufacturing and regulatory and clinical development as well as management personnel; and
- expand our operational, financial and management systems and increase personnel, including personnel to support our operations as a public company.

Based on our current cash and cash equivalents, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2020. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with research, development and commercialization of gene therapies, it is difficult to estimate with certainty the amount of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the progress, costs and results of our preclinical development and initial clinical trials for our gene therapy programs;
- the progress, costs and results of our additional clinical, research and preclinical development programs in gene therapy;
- the costs and timing of process development and manufacturing scale-up activities associated with our clinical programs;
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements;
- the scope, progress, results and costs of any product candidates that we may derive from our platform technology or any other product candidates that we may develop;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against any intellectual property-related claims.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements and marketing and distribution arrangements.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of Ordinary Shares. 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

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we raise additional funds through other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs 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 or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

### **Contractual Obligations and Commitments**

Other than the repayment of the notes payable at December 31, 2017, there were no material changes in our commitments during the three months ended September 30, 2018 under contractual obligations as disclosed in our Prospectus outside the course of normal business.

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

We have not entered into any off-balance sheet arrangements under applicable SEC rules and do not have any holdings in variable interest entities.

### **Emerging Growth Company Status**

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an “emerging growth company,” which we are, to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to take advantage of this extended transition period.

### **Item 3. Quantitative and Qualitative Disclosures About Market Risk.**

We are exposed to market risks in the ordinary course of our business. These risks primarily include foreign currency exchange rate sensitivities. However, relative to foreign currency exposures as of September 30, 2018, a 10% unfavorable movement in foreign currency exchange rates would not expose us to a significant increase in net loss. We had cash and cash equivalents of \$88.6 million as of September 30, 2018, which consist of non-interest-bearing bank deposits. Other than accounts payable and accrued expenses incurred in the ordinary course of business, we had no other debt outstanding as of September 30, 2018.

### **Item 4. Controls and Procedures.**

#### **Limitations on effectiveness of controls and procedures**

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

#### **Evaluation of disclosure controls and procedures**

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (principal financial officer), evaluated, as of the end of the period covered by this Quarterly Report on Form 10-Q, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Based on that evaluation, our Chief Executive Officer and Chief Financial Officer (principal financial officer) concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of September 30, 2018.

#### **Changes in internal control over financial reporting**

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the three months ended September 30, 2018 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

## **PART II—OTHER INFORMATION**

### **Item 1. Legal Proceedings.**

We are not subject to any material legal proceedings.

### **Item 1A. Risk Factors.**

*Investing in our common stock involves a high degree of risk. You should consider carefully the risks described below, together with the other information included or incorporated by reference in this Quarterly Report on Form 10-Q. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations.*

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

***We have incurred significant losses since inception and anticipate that we will incur continued losses for the foreseeable future, and may never achieve or maintain profitability.***

We are a clinical stage company with limited operating history. We were formed and began operations in 2015. We have never been profitable and do not expect to be profitable in the foreseeable future. We have incurred net losses since inception, including net losses of approximately \$61.8 million and \$22.4 million for the nine months ended September 30, 2018 and 2017, respectively. As of September 30, 2018, we had an accumulated deficit of approximately \$127.2 million. Since our inception, we have devoted substantially all of our resources to developing our technology platform, establishing our viral vector manufacturing facility and developing manufacturing processes, advancing the product candidates in our ophthalmology, salivary gland and neurodegenerative disease programs, building our intellectual property portfolio, organizing and staffing our company, business planning, raising capital, and providing general and administrative support for these operations. We have not yet demonstrated an ability to successfully complete a clinical program, including large-scale, pivotal clinical trials, obtain marketing approval, manufacture product at a commercial scale, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Typically, it takes about six to ten years to develop a new drug from the time it enters Phase 1 clinical trials to when it is approved for treating patients, but in many cases, it may take longer. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing genetic medicine products.

We expect to continue to incur significant expenses and additional operating losses for the foreseeable future as we seek to advance product candidates through preclinical and clinical development, expand our research and development activities, develop new product candidates, complete clinical trials, seek regulatory approval and, if we receive regulatory approval, commercialize our products. Furthermore, the costs of advancing product candidates into each succeeding clinical phase tend to increase substantially over time. The total costs to advance any of our product candidates to marketing approval in even a single jurisdiction would be substantial. Because of the numerous risks and uncertainties associated with gene therapy product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to begin generating revenue from the commercialization of products or achieve or maintain profitability. Our expenses will also increase substantially as we operate as a public company and add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, as well as to support our transition to a public reporting company.

Before we generate any revenue from product sales, each of our programs and product candidates will require additional preclinical and/or clinical development, potential regulatory approval in multiple jurisdictions, manufacturing, building of a commercial organization, substantial investment and significant marketing efforts. Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or FDA, European Medicines Agency, or EMA, or other regulatory authorities to perform preclinical studies and clinical trials in addition to those that we currently anticipate. These risks are further described under “—Risks Related to Discovery, Development, Clinical Testing, Manufacturing and Regulatory Approval” and “—Risks Related to Commercialization.” As a result, we expect to continue to incur net losses and negative cash flows for the foreseeable future. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our shareholders’ equity and working capital.

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As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any particular quarterly or annual period as indications of future operating performance. If we are unable to develop and commercialize one or more of our product candidates either alone or with collaborators, or if revenues from any product candidate that receives marketing approval are insufficient, we will not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability. If we are unable to achieve and then maintain profitability, the value of our equity securities will be adversely affected.

### ***We will require additional capital to fund our operations, which may not be available on acceptable terms, if at all.***

We expect to spend substantial amounts to complete the development of, seek regulatory approvals for and commercialize our product candidates. We will require additional capital beyond the proceeds of our IPO, which we may raise through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources to enable us to complete the development and potential commercialization of our product candidates. Furthermore, we expect to incur additional costs associated with operating as a public company. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative effect on our financial condition and our ability to pursue our business strategy. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our product candidate development efforts. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate certain of our research and development programs.

Our operations have consumed significant amounts of cash since inception. As of September 30, 2018, our cash and cash equivalents were \$88.6 million. Based on our current cash and cash equivalents, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2020. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more than currently expected because of circumstances beyond our control. Because the length of time and activities associated with successful development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the progress, timing, costs and results of our ongoing clinical development for our *CNGB3* gene therapy product candidate, AAV-CNGB3, for our *RPE65*-deficiency product candidate, AAV-RPE65, for our X-linked retinitis pigmentosa product candidate, AAV-RPGR, for our radiation induced xerostomia and Sjogren's syndrome-associated xerostomia or xerophthalmia product candidate, AAV-AQP1, and our continued ongoing natural history studies for inherited retinal diseases, or IRDs;
- the initiation of Phase 1/2 clinical trials for our *CNGA3* gene therapy product candidate, AAV-CNGA3, and for our product candidate for the treatment of xerostomia or xerophthalmia associated with *Sjogren's* syndrome, AAV-AQP1;
- future discussions with regulatory agencies and potential subsequent initiation of future clinical trials for our *GAD* gene therapy product, AAV-GAD, which we acquired pursuant to the Merger Agreement with Vector;
- continuing our current research programs, our preclinical development of product candidates from our current research programs and further developing our gene regulation technology;
- seeking to identify, assess, acquire and/or develop additional research programs and additional product candidates;
- the preclinical testing and clinical trials for any product candidates we identify and develop;
- establishing a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, EMA and other regulatory authorities;
- the cost of expanding and protecting our intellectual property portfolio, including filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions brought by third parties against us or any of our product candidates;
- the effect of competing technological and market developments;
- the cost of further developing and scaling our manufacturing facility and processes;

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- the cost and timing of completion of commercial-scale manufacturing activities;
- the cost of making royalty, milestone or other payments under current and any future in-license agreements;
- the extent to which we in-license or acquire other products and technologies;
- the cost of establishing sales, marketing and distribution capabilities for our product candidates in regions where we choose to commercialize our products; and
- the initiation, progress, timing and results of our commercialization of our product candidates, if approved for commercial sale.

We cannot be certain that additional funding will be available on acceptable terms, or at all. 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 potentially discontinue operations.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common shareholder. 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 raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required 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 or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

***We are heavily dependent on the success of our most advanced product candidates, AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, which are still in development, and if none of them receive regulatory approval or are successfully commercialized, our business may be harmed.***

To date, we have invested a significant portion of our efforts and financial resources in the development of AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1. Our future success and ability to generate product revenue is substantially dependent on our ability to successfully develop, obtain regulatory approval for and successfully commercialize these product candidates. We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We expect to invest a meaningful portion of our efforts and expenditures over the next few years in AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, which will require additional clinical development, management of clinical and manufacturing activities, regulatory approval in multiple jurisdictions, manufacturing sufficient supply, building of a commercial organization, substantial investment and significant marketing efforts before we can generate any revenues from any commercial sales. Accordingly, our business currently depends heavily on the successful development, regulatory approval and commercialization of AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, which may never occur. We cannot be certain that AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 or AAV-AQP1 will be successful in clinical trials, receive regulatory approval or be successfully commercialized even if we receive regulatory approval. Even if we receive approval to market AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 or AAV-AQP1 from the FDA, EMA or other regulatory bodies, we cannot be certain that our product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives. Additionally, the research, testing, manufacturing, labeling, approval, sale, marketing and distribution of gene therapy products are and will remain subject to extensive and evolving regulation by the FDA, EMA and other regulatory authorities. We are not permitted to market AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 or AAV-AQP1 in the United States until they receive approval of a biologics license application, or BLA, from the FDA, and we cannot market them in the European Union until we receive approval for a Marketing Authorization Application, or MAA, from the EMA, or other required regulatory approval in other countries.

AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1 are our most advanced product candidates, and because some of our other product candidates are based on similar technology, if AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 or AAV-AQP1 show unexpected adverse events or a lack of efficacy in the indications we intend to treat, or if we experience other regulatory or developmental issues, our development plans and business could be significantly harmed. Further, competitors may be developing products with similar technology and may experience problems with their products that could identify problems that would potentially harm our business.

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To date, we have not yet met with regulatory agencies nor determined the regulatory pathway and any potential related development costs for our recently acquired AAV-GAD gene therapy program for Parkinson's disease, nor are we under any obligation to do so.

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

Part of our strategy involves identifying novel product candidates. The process by which we identify product candidates may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also:

- we may not be able to assemble sufficient resources to acquire or discover additional product candidates;
- competitors may develop alternatives that render our potential product candidates obsolete or less attractive;
- potential product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- potential product candidates may, on further study, be shown to have harmful side effects, toxicities or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance;
- potential product candidates may not be effective in treating their targeted diseases;
- the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable;
- a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- the regulatory pathway for a potential product candidate is too complex and difficult to navigate successfully or economically.

In addition, we may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. As a result, we may fail to capitalize on 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. If we are unable to identify additional suitable product candidates for clinical development, this would adversely impact our business strategy and our financial position and share price and could potentially cause us to cease operations.

### **Risks Related to Discovery, Development, Clinical Testing, Manufacturing and Regulatory Approval**

***We intend to identify and develop product candidates based on our novel gene therapy platform, which makes it difficult to predict the time and cost of product candidate development. Very few products that utilize transduction technology have been approved in the United States or in Europe, and there have only been a limited number of clinical trials involving a gene therapy product candidate.***

We have concentrated a portion of our research and development efforts on our gene therapy platform, which uses both transduction and gene regulation technology. Our future success depends on the successful development of these novel therapeutic approaches. To date, very few products that utilize gene transfer have been approved in the United States or Europe. There have been a limited number of clinical trials of gene transduction technologies, with only one product candidate ever approved by the FDA.

Our gene therapy platform is based on a suite of viral vectors which we can deploy with gene therapy constructs, which relies on the ability of AAV to efficiently transmit a therapeutic gene to certain kinds of cells. The mechanism of action by which these vectors target particular tissues is still not completely understood. Therefore, it is difficult for us to determine that our vectors will be able to properly deliver gene transfer constructs to enough tissue cells to reach therapeutic levels. We cannot be certain that our viral vectors will be able to meet safety and efficacy levels needed to be therapeutic in humans or that they will not cause significant adverse events or toxicities. Furthermore, recent work conducted by a third party in non-human primates suggests that intravenous delivery of certain AAV vectors at very high doses may result in severe toxicity. The indications that we target do not use IV administration for viral vector delivery and do not use doses as high as those tested in these publications, and to date we have not observed the severe toxicities described in these publications with the naturally occurring AAV vectors that we use. However, we cannot be certain that we will be able to avoid triggering toxicities in our future preclinical studies or clinical trials. Any such results could impact our ability to develop a product candidate. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our gene therapy platform, or any similar or competitive gene therapy platforms, will result in the identification, development, and regulatory approval of any product candidates, or that other gene therapy technologies will not be considered better or more attractive. There can be no assurance that any development problems we experience in the future related to our gene therapy platform or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays and challenges in utilizing our manufacturing facility and achieving sustainable, reproducible, and scalable production. Any of these factors may prevent us from completing our preclinical studies or clinical trials or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

In addition, because our gene regulation technology is still in the research stage, we have not yet been able to assess safety in humans, and there may be long-term effects from treatment that we cannot predict at this time. Also, animal models may not exist for some of the diseases we expect to pursue.

***Because gene therapy is novel and the regulatory landscape that governs any product candidates we may develop is uncertain and may change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.***

The regulatory requirements that will govern any novel gene therapy product candidates we develop are not entirely clear and may change. Within the broader genetic medicine field, very few therapeutic products have received marketing authorization from the EMA and FDA. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and will likely continue to change in the future. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at the institution participating in the clinical trial. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the United States National Institutes of Health, or the NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee. [Should we include update per recent regulatory guidance from July 2018?] Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. The same applies in the European Union. The EMA's Committee for Advanced Therapies, or CAT, is responsible for assessing the quality, safety, and efficacy of advanced-therapy medicinal products. Advanced-therapy medicinal products include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. In the European Union, the development and evaluation of a gene therapy product must be considered in the context of the relevant EU guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any gene therapy product candidate we may develop, but that remains uncertain at this point.

Adverse developments in preclinical studies or clinical trials conducted by others in the field of gene therapy and gene regulation products may cause the FDA, the EMA, and other regulatory bodies to revise the requirements for approval of any product candidates we may develop or limit the use of products utilizing gene regulation technologies, either of which could harm our business. In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. The regulatory approval process for product candidates such as ours can be more expensive and take longer than for other, better known, or more extensively studied pharmaceutical or other product candidates. Further, as we are developing novel treatments for diseases in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the EMA or other regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. The prospectively designed natural history studies with the same endpoints as our corresponding clinical trials may not be accepted by the FDA, EMA or other regulatory authorities. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing gene regulation technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our research programs or the commercialization of resulting products.

The regulatory review committees and advisory groups described above and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates, or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future product candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of any product candidates we identify and develop.

***Clinical trials are expensive, time-consuming, difficult to design and implement, and involve an uncertain outcome. Further, we may encounter substantial delays in our clinical trials.***

The clinical trials and manufacturing of our product candidates are, and the manufacturing and marketing of our products, if approved, will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and market our product candidates. Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are both safe and effective for use in each target indication. In particular, because our product candidates are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure, and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use.

Clinical testing is expensive and can take many years to complete, and subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. Failure can occur at any time during the clinical trial process. Even if our future clinical trials are completed as planned, we cannot be certain that their results will support the safety and effectiveness of our product candidates for their targeted indications. Our future clinical trial results may not be successful.

In addition, even if such trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates.

To date, we have not completed any clinical trials required for the approval of our product candidates. Although we have already begun Phase 1/2 clinical trials, we may experience delays in conducting any clinical trials and we do not know whether our clinical trials will begin on time, need to be redesigned, recruit and enroll patients on time or be completed on schedule, or at all. Events that may prevent successful or timely completion of clinical development include:

- inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation of clinical trials;
- delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for advanced clinical trials;
- delays in developing suitable assays for screening patients for eligibility for trials with respect to certain product candidates;
- delays in reaching agreement with the FDA, EMA or other regulatory authorities as to the design or implementation of our clinical trials;
- obtaining regulatory approval to commence a clinical trial;
- reaching an agreement on acceptable terms with clinical trial sites or prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different clinical trial sites;
- obtaining institutional review board, or IRB, approval at each site;
- recruiting suitable patients to participate in a clinical trial;
- developing and validating the companion diagnostic to be used in a clinical trial, if applicable;
- having patients complete a clinical trial or return for post-treatment follow-up;
- clinical sites, contract research organizations, or other third parties deviating from trial protocol or dropping out of a trial;
- failure to perform in accordance with the FDA's good clinical practice, or GCP, requirements, or applicable regulatory guidelines in other countries;
- addressing patient safety concerns that arise during the course of a trial, including occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- adding a sufficient number of clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

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We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates or significantly increase the cost of such trials, including:

- we may experience changes in regulatory requirements or guidance, or receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials 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;
- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate and we may not have funds to cover the costs;
- 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;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- any future collaborators that conduct clinical trials may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA, EMA 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 the FDA, EMA 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 drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. For example, our IND for AAV-RPE65 was filed in July 2017. On August 16, 2017, we received notification from the FDA supporting the use of the described batches of product candidate in the Phase 1/2 clinical trial. However, we received a recommendation from the FDA on a certain aspect of the manufacturing process for future clinical trials, thus putting our IND for AAV-RPE65 on partial clinical hold. We responded to the FDA on October 2, 2017 and, based on this response, the partial clinical hold was lifted on October 17, 2017. As another example, our IND for AAV-CNGB3 was filed on October 31, 2017. We received a question from the FDA around our injection device compatibility assay, thus putting our AAV-CNGB3 IND on clinical hold. In the device compatibility assay, the FDA noted a disparity between the target titer for the intended low dose dilution and the actual titer obtained on polymerase chain reaction, or PCR, analysis. The FDA requested clarification on whether this was an imprecise dilution scheme for the low dose or a PCR assay issue. We submitted our second response to the FDA on May 2, 2018 providing data that identified the issue as a PCR assay artifact and also showing data that we believe supports that this has now been addressed. On May 31, 2018 the FDA released the clinical hold on our IND for AAV-CNGB3.

Our most advanced product candidates, AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65 and AAV-AQP1, will require extensive clinical testing before we are prepared to submit a BLA or MAA for regulatory approval. We cannot predict with any certainty if or when we might complete the clinical development for our product candidates and submit a BLA or MAA for regulatory approval of any of our product candidates or whether any such BLA or MAA will be approved. We may also seek feedback from the FDA, EMA or other regulatory authorities on our clinical development program, and the FDA, EMA or such regulatory authorities may not provide such feedback on a timely basis, or such feedback may not be favorable, which could further delay our development programs.

If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our product candidates could be harmed, and our ability to generate revenues from our product candidates may be delayed. In addition, any delays in our clinical trials could increase our costs, slow down the development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and results of operations. In addition, 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.

***The affected populations for our other product candidates may be smaller than we or third parties currently project, which may affect the addressable markets for our product candidates.***

Our projections of the number of people who have the diseases we are seeking to treat, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are estimates based on our knowledge and understanding of these diseases. The total addressable market opportunity for our product candidates will ultimately depend upon a number of factors including the diagnosis and treatment criteria included in the final label, if approved for sale in specified indications, acceptance by the medical community, patient access and product pricing and reimbursement. Incidence and prevalence estimates are frequently based on information and assumptions that are not exact and may not be appropriate, and the methodology is forward-looking and speculative. The process we have used in developing an estimated incidence and prevalence range for the indications we are targeting has involved collating limited data from multiple sources. Accordingly, the incidence and prevalence estimates included, or supporting the information, in this Quarterly Report on Form 10-Q should be viewed with caution. Further, the data and statistical information included, or supporting the information, in this Quarterly Report on Form 10-Q including estimates derived from them, may differ from information and estimates made by our competitors or from current or future studies conducted by independent sources.

The use of such data involves risks and uncertainties and is subject to change based on various factors. Our estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of the diseases we seek to address. The number of patients with the diseases we are targeting in the United States, the European Union and elsewhere may turn out to be lower than expected or may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or access, all of which would harm our results of operations and our business.

***Negative public opinion of gene therapy and increased regulatory scrutiny of gene therapy and genetic research may adversely impact public perception of our current and future product candidates.***

Our potential therapeutic products involve introducing genetic material into patient's cells. The clinical and commercial success of our potential products will depend in part on public acceptance of the use of gene therapy and gene regulation for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy and gene regulation are unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products once approved. For example, in 2003, trials using early versions of murine gamma-retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events, including reported cases of leukemia. Although none of our current product candidates utilize murine gamma-retroviral vectors, our product candidates use a viral delivery system. Adverse events in our clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental 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 candidates. The risk of cancer remains a concern for gene therapy and we cannot assure that it will not occur in any of our planned or future clinical trials. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. If any such adverse events occur, commercialization of our product candidates or further advancement of our clinical trials could be halted or delayed, which would have a negative impact on our business and operations.

***Even though we have been granted access to the PRIME scheme by the EMA for AAV-CNGB3 and the FDA granted Fast Track designation to AAV-RPGR and AAV-CNGB3, in the future we may seek and fail to obtain access to the PRIME scheme by the EMA or fast track designation by the FDA for other of our current or potential future product candidates. We may also seek and fail to obtain breakthrough therapy designation from the FDA for our current or any future product candidates. Such designations or access may also not lead to faster development or regulatory review or approval, and it does not increase the likelihood that our product candidates will receive marketing approval.***

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of new drugs and biological products that meet certain criteria. For example, the FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs, or if the drug has been designated as a qualified infectious disease product. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. Under Fast Track, the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted if relevant criteria are satisfied, including an agreement with FDA on the proposed schedule for the submission of portions of the BLA, and the payment of applicable user fees before FDA may initiate a review. Even if Fast Track designation is granted, it may be rescinded if the product no longer meets the qualifying criteria. In April 2018, AAV-RPGR was designated a Fast Track program by the FDA for the treatment of X-linked retinitis pigmentosa owing to defects in *RPGR*. In August 2018, AAV-CNGB3 was granted fast track designation by the FDA for the treatment of achromatopsia associated with defects in *CNGB3*.

In 2012, the Food and Drug Administration Safety and Innovation Act, or FDASIA, established the breakthrough therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically-significant endpoints, such as substantial treatment effects observed early in clinical development. Sponsors may request that FDA designate a product candidate as a breakthrough therapy at the time of or any time after the submission of an IND, but ideally before an end-of-phase II meeting with FDA. If the FDA designates a breakthrough therapy, it may take actions appropriate to expedite the development and review of the application, which may include but are not limited to holding meetings with the sponsor and the review team throughout the development of the therapy; providing timely advice to, and interactive communication with, the sponsor regarding the development of the product candidate to ensure collection of appropriate data needed to support approval; more frequent written correspondence from the FDA about such things as the design of the proposed clinical trials and use of biomarkers; intensive guidance on an efficient drug development program, beginning as early as Phase 1; organizational commitment involving senior managers; and eligibility for rolling review and priority review. Breakthrough therapy designation comes with all of the benefits of fast track designation, which means that the sponsor may file sections of the BLA for review on a rolling basis if certain conditions are satisfied, including an agreement with FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review. Fast Track designation, priority review and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process.

Similarly, the EMA has established the PRIME scheme to expedite the development and review of product candidates that show a potential to address to a significant extent an unmet medical need, based on early clinical data. In February 2018, AAV-CNGB3 in the treatment of achromatopsia associated with defects in *CNGB3* was admitted to the PRIME scheme of the EMA.

Fast Track designation and designation as a breakthrough therapy are within the discretion of the FDA. Accordingly, even if we believe one of our other product candidates meets the criteria for Fast Track designation or designation as a breakthrough therapy and we seek such designation, the FDA may disagree and instead determine not to make such designation for such product candidate. We cannot be sure that our evaluation of our product candidates as qualifying for Fast Track designation or breakthrough therapy designation will meet the FDA's expectations. In any event, the receipt of a Fast Track designation or breakthrough therapy designation for a product candidate may not result in a faster development process, review, or approval compared to product candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if additional product candidates are granted Fast Track designation or one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Similarly, access to the PRIME scheme is at the discretion of the EMA, and we cannot be sure that any additional current or future product candidates will be granted access to the scheme; that participation in the scheme will result in expedited regulatory review or approval of our product candidates; or that access to the scheme, once granted, will not be revoked.

***We have received orphan drug designation from the FDA and EMA for AAV-CNGA3, AAV-CNGB3, AAV-RPE65, AAV-RPGR, AAV-AIPL1 and FDA for AAV-AQP1 and may seek orphan drug designation for additional product candidates in the future, but any orphan drug designations we have received or may receive in the future may not confer marketing exclusivity or other expected benefits.***

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as one occurring in a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating, or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax credits for qualified clinical testing, and user-fee waivers. In addition, if a product receives the first FDA approval of that drug for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the rare disease or condition. Under the FDA's regulations, the FDA will deny orphan drug exclusivity to a designated drug upon approval if the FDA has already approved another drug with the same active ingredient for the same indication, unless the drug is demonstrated to be clinically superior to the previously approved drug. In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following approval for the approved therapeutic indication. This period may be reduced to six years if, at the end of the fifth year, the orphan drug designation criteria are no longer met, including where it is shown that the drug is sufficiently profitable not to justify maintenance of market exclusivity. In the European Union, a marketing authorization for an orphan designated product will not be granted if a similar drug has been approved in the European Union for the same therapeutic indication, unless the applicant can establish that its product is safer, more effective or otherwise clinically superior. A similar drug is a product containing a similar active substance or substances as those contained in an already authorized product. Similar active substance is defined as an identical active substance, or an active substance with the same principal molecular structural features (but not necessarily all of the same molecular features) and which acts via the same mechanism.

We have obtained orphan drug designation from the FDA and European Commission for AAV-CNGB3 for the treatment of achromatopsia caused by mutations in the *CNGB3* gene, AAV-RPE65 for the treatment of Leber congenital amaurosis, AAV-RPGR for the treatment of retinitis pigmentosa and AAV-AIPL1 for the treatment of inherited retina dystrophy due to defects in *AIPL1* gene, and we obtained orphan drug designation from the FDA for AAV-AQP1 for the treatment of grade 2 and grade 3 late xerostomia from parotid gland hypofunction caused by radiotherapy or Sjögren's syndrome-associated xerostomia or xerophthalmia. We have been granted orphan drug designation and rare pediatric disease designation by the FDA and received a positive opinion from the EMA Committee for Orphan Medicinal Products recommending orphan medicinal product (orphan drug) designation in the EU for our AAV-CNGA3 program for treatment of achromatopsia caused by mutations in the *CNGA3* gene. We plan to seek orphan drug designation for other current and future product candidates. Even with orphan drug designation, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products, which could prevent us from marketing our product candidates if another company is able to obtain orphan drug exclusivity before we do. In addition, exclusive marketing rights in the United States may be unavailable if we seek approval for an indication broader than the orphan-designated indication or may be lost in the United States if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the drug to meet the needs of patients with the rare disease or condition following approval. Further, even if we obtain orphan drug exclusivity, that exclusivity may not effectively protect our product candidates from competition because different drugs with different active moieties can be approved for the same condition. In addition, the FDA and the EMA can subsequently approve products with the same active moiety for the same condition if the FDA or the EMA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, while we intend to seek orphan drug designation for other existing and future product candidates, we may never receive such designations. There have been legal challenges to aspects of the FDA's regulations and policies concerning the exclusivity provisions of the Orphan Drug Act, and future challenges could lead to changes that affect the protections afforded our product candidates in ways that are difficult to predict. In 2014, a U.S. district court invalidated the FDA's denial of orphan exclusivity to an orphan designated drug, which the FDA had based on its determination that the drug was not proven to be clinically superior to a previously approved "same drug." In response to the decision, the FDA released a policy statement stating that the court's decision is limited to the facts of that particular case and that the FDA will continue to deny orphan drug exclusivity to a designated drug upon approval if the drug is the "same" as a previously approved drug, unless the drug is demonstrated to be clinically superior to that previously approved drug. Since then, similar legal challenges have been initiated against the FDA for its denial of orphan drug exclusivity to other designated drugs, and in 2017, Congress amended the Orphan Drug Act to require a

demonstration of clinical superiority upon approval as a condition of receiving orphan drug exclusivity when another “same drug” has already been approved for the same indication. In the future, there is the potential for additional legal challenges to the FDA’s orphan drug regulations and policies, and it is uncertain how ongoing and future challenges might affect our business.

***We and our contract manufacturer for plasmid are subject to significant regulation with respect to manufacturing our products. Our manufacturing facilities and the third-party manufacturing facility which we rely on may not continue to meet regulatory requirements and have limited capacity.***

We currently have relationships with a limited number of suppliers for the manufacturing of plasmid, a component of our viral vectors and product candidates. We completed the fit-out of our cGMP manufacturing facility in early 2018. However, if we experience slowdowns or problems with our facility and are unable to establish or scale our internal manufacturing capabilities, we will need to continue to contract with manufacturers that can produce the preclinical, clinical and commercial supply of our products. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities.

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers for components our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials in the European Union must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA or MAA on a timely basis. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could harm our business. If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition and results of operations may be harmed. Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through a BLA and/or MAA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

***Any contamination in our manufacturing process, shortages of raw materials or failure of our plasmid supplier to deliver necessary components could result in delays in our clinical development or marketing schedules.***

Given the nature of biologics manufacturing, there is a risk of contamination. Any contamination could adversely affect our ability to produce product candidates on schedule and could, therefore, harm our results of operations and cause reputational damage. Some of the raw materials required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could adversely affect our development timelines and our business, financial condition, results of operations and prospects.

***If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.***

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. The natural history studies may fail to provide us with patients for our clinical trials because patients enrolled in the natural history studies may not be good candidates for our clinical trials, or may choose to not enroll in our clinical trials. We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. The enrollment of patients depends on many factors, including:

- the size and nature of the patient population;
- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our clinical trials may compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates or approved products for the same clinical indications, and this competition may reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors, or chose to be treated using Luxturna, a commercially available product by Spark Therapeutics, Inc. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which may reduce the number of patients who are available for our clinical trials in such clinical trial site.

Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our product candidates, or could render further development impossible.

***Our product candidates may cause serious adverse events or undesirable side effects or have other properties which may delay or prevent their regulatory approval, limit the commercial profile of an approved label, or, result in significant negative consequences following marketing approval, if any.***

Serious adverse events or undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA or other authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects, toxicities or unexpected characteristics, including death. A risk in any gene therapy product based on viral vectors is the risk of insertional oncogenesis.

If unacceptable side effects or deaths arise in the development of our product candidates, we, the FDA, the IRBs at the institutions in which our studies are conducted, DSMB, EMA or CAT could suspend or terminate our clinical trials or the FDA, EMA or other regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Undesirable side effects or deaths in clinical trials with our product candidates may cause the FDA or comparable foreign regulatory authorities to place a clinical hold on the associated clinical trials, to require additional studies, or otherwise to delay or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

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If any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by any such product, including during any long-term follow-up observation period recommended or required for patients who receive treatment using our products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product;
- regulatory authorities may require additional warnings on the label, such as a “black box” warning or contraindication;
- we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- the product could become less competitive;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

### ***Success in preclinical studies or clinical trials may not be indicative of results in future clinical trials.***

Results from previous preclinical studies or clinical trials are not necessarily predictive of future clinical trial results, and interim results of a clinical trial are not necessarily indicative of final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Frequently, product candidates that have shown promising results in early clinical trials have subsequently suffered significant setbacks in later clinical trials. In addition, the design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. There is a high failure rate for drugs and biologic products proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

### ***The regulatory approval processes of the FDA, EMA and other regulatory authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.***

The time required to obtain approval by the FDA, EMA and other regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our product candidates in clinical programs or any other product candidates we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States or the European Union until we receive regulatory approval of a BLA from the FDA or a MAA from the EMA, respectively. It is possible that the FDA may refuse to accept for substantive review any biologic license applications, or BLAs, or the EMA any of our MAAs, that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates.

Prior to obtaining approval to commercialize a product candidate in the United States, the European Union or elsewhere, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA, EMA or foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA, EMA or other regulatory authorities. The FDA or EMA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program. Depending on the extent of these or any other FDA or EMA required studies, approval of any regulatory approval applications that we submit may be delayed by several years, or may require us to expend significantly more resources than we have available.

Of the large number of potential products in development, only a small percentage successfully complete the FDA, EMA or other foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

***Even if we obtain FDA or EMA approval for AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65, AAV-AQP1 or AAV-GAD in the United States or European Union, we may never obtain approval for or commercialize it in any other jurisdiction, which would limit our ability to realize their full market potential.***

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy. Approval by the FDA in the United States or the EMA in the European Union does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

***Even if we receive regulatory approval of our product candidates, 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.***

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, advertising and promotional activities for such product, among other things, will be subject to extensive and ongoing requirements of and review by the FDA, EMA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and drug listing requirements, continued compliance with cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping and GCP requirements for any clinical trials that we conduct post-approval.

The FDA and EMA closely regulate the post-approval marketing and promotion of genetic therapy medicines to ensure they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and EMA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market our products for uses beyond their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the U.S. federal Food, Drug, and Cosmetic Act, or FDCA, relating to the promotion of prescription drugs may lead to FDA enforcement actions and investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

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In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, 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 yield various results, including:

- restrictions on manufacturing such products;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or holds on clinical trials;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure or detention; or
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and biologics and spur innovation and contains provisions applicable to the development of gene therapies, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. 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.

***Interim "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, we may publish interim "top-line" or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

***We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

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

#### **Risks Related to Healthcare Laws and Other Legal Compliance Matters**

***Enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.***

In the United States, the European Union and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- new requirements to report certain financial arrangements with physicians and teaching hospitals, including reporting “transfers of value” made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members;
- 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;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer’s Medicaid rebate liability;
- a licensure framework for follow on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Most recently, the Tax Cuts and Jobs Act of 2017 was enacted, which includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. The current Trump administration and Congress will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. It is uncertain the extent to which any such changes may impact our business or financial condition.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, led to aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute will remain in effect through 2027 unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers and accordingly, our financial operations.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. The Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, on May 11, 2018, President Trump laid out his administration's "Blueprint" to reduce the cost of prescription drugs while preserving innovation and cures. The Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. Although some of these, and other, proposals will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize our product candidates, if approved.

In markets outside of the United States and the European Union, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States, the European Union or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

***Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.***

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, 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 U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal civil and criminal false claims and civil monetary penalties laws, including the civil False Claims Act, which prohibit, among other things, , including through civil whistleblower or qui tam actions, individuals or entities from knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. 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 U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes which prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. 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 its implementing regulations, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as certain health plans, healthcare clearinghouses and healthcare providers as well as their business associates, independent contractors of a covered entity that perform certain services involving the use or disclosure of individually identifiable health information;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. Public Health Service Act, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program, with specific exceptions, to report annually to the government information related to certain payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- similar healthcare laws and regulations in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

***We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities.***

Our operations, including our development, testing and manufacturing activities, are subject to numerous environmental, health and safety laws and regulations. These laws and regulations govern, among other things, the controlled use, handling, release and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds and compounds that have a toxic effect on reproduction, laboratory procedures and exposure to blood-borne pathogens. If we fail to comply with such laws and regulations, we could be subject to fines or other sanctions.

As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, the production efforts of our third-party manufacturers or our development efforts may be interrupted or delayed.

***Due to our international operations, we are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses.***

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act; the U.S. Foreign Corrupt Practices Act, or FCPA; and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Bribery Act, FCPA, and these other laws generally prohibit us, our officers and our employees and intermediaries from bribing, being bribed by, or providing prohibited payments or anything else of value to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, FCPA, or local anti-corruption laws. In addition, we cannot predict the nature, scope, or effect of future regulatory requirements to which any of our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We also are subject to other laws and regulations governing any international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the EU, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, or, collectively, the Trade Control laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA, or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA, and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement, and other sanctions and remedial measures and legal expenses. Any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws, or Trade Control laws by U.K., U.S., or other authorities, even if it is ultimately determined that we did not violate such laws, could be costly and time-consuming, require significant personnel resources, and harm our reputation.

We will seek to build and continuously improve our systems of internal controls and to remedy any weaknesses identified. There can be no assurance, however, that the policies and procedures will be followed at all times or effectively detect and prevent violations of the applicable laws by one or more of our employees, consultants, agents, or collaborators and, as a result, we could be subject to fines, penalties, or prosecution.

### **Risks Related to Commercialization**

***We face significant competition in an environment of rapid technological change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may harm our financial condition and our ability to successfully market or commercialize any product candidates we may develop.***

The development and commercialization of new gene therapy products is highly competitive. Moreover, the gene regulation and manufacturing fields are characterized by rapidly changing technologies, significant competition, and a strong emphasis on intellectual property. We will face competition with respect to any product candidates that we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs, including inherited retinal diseases and neurodegenerative diseases. Some of these competitive products and therapies are based on scientific approaches that are similar to our approach, and others are based on entirely different approaches.

Our platform and products focus on the development of gene therapies and gene regulation technology. There are a number of companies developing ocular gene therapy products including Applied Genetic Technologies Corporation, Nightstar Therapeutics plc and Spark Therapeutics, Inc. There are a number of companies developing gene therapy products for neurodegenerative diseases, including Voyager Therapeutics, Inc. and Axovant Sciences Ltd. In addition to competition from other gene therapies, any products we may develop may also face competition from other types of therapies, such as small molecule, antibody, protein or other therapies.

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

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

***The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.***

The availability of coverage and adequacy of reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates, assuming FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement for our products or procedures using our products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates. Obtaining coverage and adequate

reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. Separate reimbursement for the product itself or the treatment or procedure in which our product is used may not be available. A decision by a third-party payor not to cover or separately reimburse for our products or procedures using our products, could reduce physician utilization of our products once approved. Assuming there is coverage for our product candidates or procedures using our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the European Union or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly-approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially-reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States 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 our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

***Even if our product candidates receive marketing approval, they may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success.***

If our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If they do not achieve an adequate level of acceptance, we may not generate significant product revenues or become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the efficacy and potential advantages compared to alternative treatments;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement;
- product labeling or product insert requirements of the FDA, EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our product together with other medications.

Because we expect sales of our product candidates, if approved, to generate substantially all of our product revenues for a substantial period, the failure of this product to find market acceptance would harm our business and could require us to seek additional financing.

***If we are unable to establish sales, marketing and distribution capabilities either on our own or in collaboration with third parties, we may not be successful in commercializing our product candidates or realizing the synergies in the target indications of our programs, even if they are approved.***

We do not have any infrastructure for the sales, marketing or distribution of our products, and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. We expect to build a focused sales, distribution and marketing infrastructure to market our product candidates in the United States and European Union, if approved. There are significant expenses and risks involved with establishing our own sales, marketing and distribution capabilities, including our ability to hire, retain and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could delay any product launch, which would adversely impact the commercialization of our product candidates. Additionally, if the commercial launch of our product candidates 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.

We may not have the resources in the foreseeable future to allocate to the sales and marketing of our product candidates in certain international markets. Therefore, our future sales in these markets will largely depend on our ability to enter into and maintain collaborative relationships for such capabilities, the collaborator's strategic interest in the product and such collaborator's ability to successfully market and sell the product. We may pursue collaborative arrangements regarding the sale and marketing of AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65, AAV-AQP1 and AAV-GAD, if approved, for the U.S. and/or certain markets overseas; however, we cannot assure that we will be able to establish or maintain such collaborative arrangements, or if able to do so, that they will have effective sales forces.

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If we are unable to build our own sales force or negotiate a collaborative relationship for the commercialization of AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65, AAV-AQP1 and AAV-GAD we may be forced to delay the potential commercialization of AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65, AAV-AQP1 and AAV-GAD or reduce the scope of our sales or marketing activities for AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65, AAV-AQP1 and AAV-GAD. If we elect to increase our expenditures to fund commercialization activities internationally, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. We could enter into arrangements with collaborative partners at an earlier stage than otherwise would be ideal and we may be required to relinquish rights to AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65, AAV-AQP1 and AAV-GAD or otherwise agree to terms unfavorable to us, any of which may have an adverse effect on our business, operating results and prospects.

Some indications targeted by our ophthalmology programs are rare, but we anticipate realizing synergies in commercializing of our IRD product candidates, should they be approved. Failure to realize synergies in our sales, marketing and distribution efforts may harm our commercialization efforts.

If we are unable to establish adequate sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65, AAV-AQP1 and AAV-GAD and may not become profitable and may incur significant additional losses. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

### ***If we obtain approval to commercialize any products outside of the United States or the European Union, a variety of risks associated with international operations could adversely affect our business.***

If AAV-CNGB3, AAV-CNGA3, AAV-RPGR, AAV-RPE65, AAV-AQP1, and AAV-GAD are approved for commercialization, we intend to enter into agreements with third parties to market them in certain jurisdictions outside the United States and the European Union. We expect that we will be subject to additional risks related to international pharmaceutical operations, including:

- different regulatory requirements for drug and biologic approvals and rules governing drug and biologic commercialization in foreign countries;
- reduced protection for intellectual property rights;
- foreign reimbursement, pricing and insurance regimes;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods and fires, or from economic or political instability;
- greater difficulty with enforcing our contracts;
- potential noncompliance with the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act 2010 and similar anti-bribery and anticorruption laws in other jurisdictions; and
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by individual countries in Europe with which we will need to comply. If we are unable to successfully manage the challenges of international expansion and operations, our business and operating results could be harmed.

### ***Any product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.***

The ACA includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product

containing the sponsor's own pre-clinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have an adverse effect on the future commercial prospects for our biological products.

There is a risk that any of our product candidates approved as a biological product under a BLA would not qualify for the 12-year period of exclusivity or that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

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

***If our recently completed cGMP manufacturing facility is unable to supply our product candidates for all of our current preclinical, clinical and potential commercial needs, we will be forced to seek out third-party manufacturers. We currently contract with third parties for the manufacture of plasmid used in producing our product candidates. Relying on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.***

We have begun producing our product candidates in our facility. However, if our facility is damaged, suffers any form of delay or regulatory challenges, or we are unable to scale our internal manufacturing capabilities to meet demand for our product candidates, we will need to contract with third-party manufacturers to produce our product candidates.

We currently rely on third-party manufacturers for the manufacture of plasmid used in the production of our product candidates. We do not have a long-term supply agreement with any of the third-party manufacturers, and we purchase our required supply on a purchase order basis.

We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements that might be required by the FDA or EMA. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could adversely affect supplies of our candidates and harm our business, financial condition, results of operations, and prospects.

Any therapies that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval.

Our current and anticipated future dependence upon others for the manufacture of any product candidates we may develop or any components required for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

***We may collaborate with third parties for the development and commercialization of our product candidates. We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize our product candidates successfully, if at all.***

We may seek collaborative relationships for the development and commercialization of our product candidates. Failure to obtain a collaborative relationship for our product candidates may significantly impair their commercial potential. We also may need to enter into collaborative relationships to provide funding to support our other research and development programs. The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty, such as:

- a collaboration partner may shift its priorities and resources away from our product candidates due to a change in business strategies, or a merger, acquisition, sale or downsizing;
- a collaboration partner may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- a collaboration partner may cease development in therapeutic areas which are the subject of our strategic collaboration;
- a collaboration partner may not devote sufficient capital or resources towards our product candidates;
- a collaboration partner may change the success criteria for a product candidate thereby delaying or ceasing development of such candidate;
- a significant delay in initiation of certain development activities by a collaboration partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- a collaboration partner could develop a product that competes, either directly or indirectly, with our product candidate;
- a collaboration partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- a collaboration partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- a collaboration partner may terminate a strategic alliance;
- a dispute may arise between us and a partner concerning the research, development or commercialization of a product candidate resulting in a delay in milestones, royalty payments or termination of an alliance and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and
- a partner may use our products or technology in such a way as to make us subject to litigation with a third party.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing or commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of capital. Moreover, any collaborative partners we enter into agreements with in the future may shift their priorities and resources away from our product candidates or seek to renegotiate or terminate their relationships with us.

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

***We depend on proprietary technology licensed from others. If we lose our existing licenses or are unable to acquire or license additional proprietary rights from third parties, we may not be able to continue developing our product candidates.***

We currently in-license certain intellectual property from UCL Business, Plc, or UCLB, and Brandeis University, or Brandeis. We are a party to agreements with UCL for certain technology and AAV vector-related patents and with Brandeis for certain preclinical technology for the treatment of ALS, and we may enter into additional agreements, including license agreements, with other parties in the future that impose diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations on us. For example, in exchange for the rights granted to us by UCL, we are obligated to pay an annual management fee, milestone payments for certain commercial sales thresholds, and a certain percentages of proceeds on sublicensing revenues. If we fail to comply with our obligations to UCL, Brandeis, or any of our other collaborators, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product candidate that is covered by these agreements, which could adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

We may rely on other third parties from whom we license proprietary technology to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them. We may have limited control over these activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We may have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that may be licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than if we conduct them ourselves. 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. Furthermore, we may be unable to in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties, which we identify as necessary for our product candidates.

***If we are unable to obtain and maintain patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.***

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our proprietary technologies, product candidate development programs and product candidates. Our success depends in large part on our ability to secure and maintain patent protection in the United States and other countries with respect to our current product candidates and any future product candidates we may develop. We seek to protect our proprietary position by filing or collaborating with our licensors to file patent applications in the United States and abroad related to our proprietary technologies, development programs and product candidates. 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 or in a timely manner. Moreover, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

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. We may not have the right to control the preparation, filing, and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our proprietary products and technology, including current product candidates, any future product candidates we may develop, and our gene regulation technology in the United States or in other foreign countries, in whole or in part. Alternately, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technologies. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can prevent a patent from issuing from a pending patent application or later invalidate or narrow the scope of an issued patent. For example, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Even if patents do successfully issue and even if such patents cover our current product candidates, any future product candidates we may develop and our gene regulation technology, third parties may challenge their validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful challenge to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any of our product candidates or gene regulation technology. Our competitors may be able to circumvent our patents by developing similar or alternative product candidates in a non-infringing manner. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate and our gene regulation technology under patent protection could be reduced.

If the patent applications we hold or have in-licensed with respect to our development programs and product candidates fail to issue, if their validity, breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for any of our current or future product candidates or technology, it could dissuade companies from collaborating with us to develop product candidates, encourage competitors to develop competing products or technologies and threaten our ability to commercialize future product candidates. Any such outcome could harm our business.

The patent position of biotechnology and pharmaceutical companies is highly uncertain, involves complex legal and factual questions, and is characterized by the existence of large numbers of patents and frequent litigation based on allegations of patent or other intellectual property infringement or violation. In addition, the laws of jurisdictions outside the United States may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. Since patent applications in the United States and other jurisdictions are confidential for a period of time after filing, we cannot be certain that we were the first to file for patents covering our inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in the issuance of patents, or may result in the issuance of patents which fail to protect our technology or products, in whole or in part, or which fail to effectively prevent others from commercializing competitive technologies and products.

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 United States and abroad. 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 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. Thus, even if our patent applications issue as patents, they may not issue in a form that will provide us with meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however the life of a patent, and the protection it affords, is limited. Without patent protection for our current or future product candidates, we may be open to competition from generic versions of such 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.

***Third parties may assert claims against us alleging infringement of their patents and proprietary rights, or we may need to become involved in lawsuits to defend or enforce our patents, either of which could result in substantial costs or loss of productivity, delay or prevent the development and commercialization of our product candidates, prohibit our use of proprietary technology or sale of products or put our patents and other proprietary rights at risk.***

Our commercial success depends, in part, upon our ability to develop, manufacture, market and sell our product candidates without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Litigation relating to infringement or misappropriation of patent and other intellectual property rights in the pharmaceutical and biotechnology industries is common, including patent infringement lawsuits, interferences, oppositions and *inter partes* reviews, and reexamination proceedings before the U.S. Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. The various markets in which we plan to operate are subject to frequent and extensive litigation regarding patents and other intellectual property rights. In addition, many companies in intellectual property-dependent industries, including the biotechnology and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. Numerous U.S., EU and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates, and as the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us.

We may be subject to third-party claims including infringement, interference or derivation proceedings, post-grant review and *inter partes* review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Even if such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize the applicable product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. There may be third-party patents or patent applications with claims to compositions, formulations, or methods of treatment, prevention use, or manufacture of our product candidates or technologies. Because patent applications can take many years to issue, there may be currently pending patent applications which 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 infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover aspects of our compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to prohibit our use of those compositions, formulations, methods of treatment, prevention or use or other technologies, effectively blocking our ability to develop and commercialize the applicable product candidate until such patent expires or is finally determined to be invalid or unenforceable or unless we obtained a license.

In addition, defending such claims would cause us to incur substantial expenses and, if successful, could cause us to pay substantial damages if we are found to be infringing a third party's patent rights. These damages potentially include increased damages (possibly treble damages) and attorneys' fees if we are found to have infringed such rights willfully. Further, if a patent infringement suit is brought against us or our third-party service providers, our development, manufacturing or sales activities relating to the product or product candidate that is the subject of the suit may be delayed or terminated. As a result of patent infringement claims, or in order to avoid potential infringement claims, we may choose to seek, or be required to seek, a license from the third party, which may require payment of substantial royalties or fees, or require us to grant a cross-license under our intellectual property rights. These licenses may not be available on reasonable terms or at all. Even if a license can be obtained on reasonable terms, the rights may be nonexclusive, which would give our competitors access to the same intellectual property rights. If we are unable to enter into a license on acceptable terms, we could be prevented from commercializing one or more of our product candidates, or forced to modify such product candidates, or to cease some aspect of our business operations, which could harm our business significantly. We might also be forced to redesign or modify our product candidates so that we no longer infringe the third-party intellectual property rights, which may result in significant cost or delay to us, or which redesign or modification could be impossible or technically infeasible. Even if we were ultimately to prevail, any of these events could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business. In addition, if the breadth or strength of protection provided the patents and patent applications we own or in-license is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Competitors may infringe our patents or other intellectual property. If we or one of our licensors were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and in Europe, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness lack of written description, or non-enablement. Third parties might allege unenforceability of our patents because during prosecution of the patent an individual connected with such prosecution withheld relevant information, or made a misleading statement. Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution, but that an adverse third party may identify and submit in support of such assertions of invalidity. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Our patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors view these announcements in a negative light, the price of our Ordinary Shares could be adversely affected. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace.

***We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might adversely affect our ability to develop, manufacture and market our product candidates.***

We cannot guarantee that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, analysis of the scope of relevant patent claims or determination of the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, in the United States, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States, the European Union and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates could be filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. After issuance, the scope of patent claims remains subject to construction as determined by an interpretation of the law, the written disclosure in a patent and the patent's

prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. We may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States, the European Union or elsewhere that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

If we fail to correctly identify or interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay monetary damages, we may be temporarily or permanently prohibited from commercializing our product candidates. We might, if possible, also be forced to redesign our product candidates in a manner that no longer infringes third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

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

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and genetic medicine industries involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biotechnology and genetic medicine patents is costly, time-consuming and inherently uncertain. In addition, the Leahy-Smith America Invents Act, or the AIA, which was passed in September 2011, resulted in significant changes to the U.S. patent system.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned from a "first-to-invent" to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application and diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action.

Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. It is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents.

We may become involved in opposition, interference, derivation, *inter partes* review or other proceedings challenging our or our licensors' patent rights, and the outcome of any proceedings are highly uncertain. An adverse determination in any such proceeding could reduce the scope of, or invalidate, our owned or in-licensed patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations, and there are other open questions under patent law that courts have yet to decisively address. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways and could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution, but, the complexity and uncertainty of European patent laws has also increased in recent years. Complying with these laws and regulations could limit our ability to obtain new patents in the future that may be important for our business.

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

The USPTO, European and other patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO, European and other patent agencies over the lifetime of a patent. While an inadvertent failure to make payment of such fees or to comply with such provisions can in many cases be cured by additional payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance with such provisions will result in the abandonment or lapse of the patent or patent application, and the partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents within prescribed time limits. If we or our licensors fail to maintain the patents and patent applications covering our product candidates or if we or our licensors otherwise allow our patents or patent applications to be abandoned or lapse, it can create opportunities for competitors to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved.

***We enjoy only limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world.***

Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In-licensing patents covering our product candidates in all countries throughout the world may similarly be prohibitively expensive, if such opportunities are available at all. And in-licensing or filing, prosecuting and defending patents even in only those jurisdictions in which we develop or commercialize our product candidates may be prohibitively expensive or impractical. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection or licensed patents to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but enforcement is not as strong as that in the United States or the European Union. These products may compete with our product candidates, and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications while they are still pending. The grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications may be rejected by the relevant patent office, while substantively similar applications are granted by others. For example, relative to other countries, China has a heightened requirement for patentability and specifically requires a detailed description of medical uses of a claimed drug. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States and the European Union, and many companies have encountered significant difficulties in protecting and defending proprietary rights in such jurisdictions. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets or other forms of intellectual property, which could make it difficult for us to prevent competitors in some jurisdictions from marketing competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, are likely to result in substantial costs and divert our efforts and attention from other aspects of our business, and additionally could put at risk our or our licensors' patents of being invalidated or interpreted narrowly, could increase the risk of our or our licensors' patent applications not issuing, or could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, while damages or other remedies may be awarded to the adverse party,

which may be commercially significant. If we prevail, damages or other remedies awarded to us, 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. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition in those jurisdictions.

In some jurisdictions, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties under patents relevant to our business, or if we or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions.

***Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.***

The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. Even if we or our licensors obtain patents covering our product candidates, when the terms of all patents covering a product expire, our business may become subject to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review and approval of new product candidates, patents protecting such candidates may 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.

***If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of marketing exclusivity for our product candidates, our business may be harmed.***

In the United States, a patent that covers an FDA-approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. In the European Union, our product candidates may be eligible for term extensions based on similar legislation. In either jurisdiction, however, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial.

***Our proprietary rights may not adequately protect our technologies and product candidates, and do not necessarily address all potential threats to our competitive advantage.***

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

- others may be able to make products that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- others, including inventors or developers of our owned or in-licensed patented technologies who may become involved with competitors, may independently develop similar technologies that function as alternatives or replacements for any of our technologies without infringing our intellectual property rights;

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- we or our licensors or our other collaboration partners might not have been the first to conceive and reduce to practice the inventions covered by the patents or patent applications that we own, license or will own or license;
- we or our licensors or our other collaboration partners might not have been the first to file patent applications covering certain of the patents or patent applications that we or they own or have obtained a license, or will own or will have obtained a license;
- we or our licensors may fail to meet obligations to the U.S. government with respect to in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents;
- issued patents that we own or exclusively license may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- ownership, validity or enforceability of our or our licensors' patents or patent applications may be challenged by third parties; and
- the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business.

***Our reliance on third parties may require us to share our trade secrets, which increases the possibility that our trade secrets will be misappropriated or disclosed, and confidentiality agreements with employees and third parties may not adequately prevent disclosure of trade secrets and protect other proprietary information.***

We consider proprietary trade secrets, confidential know-how and unpatented know-how to be important to our business. We may rely on trade secrets and confidential know-how to protect our technology, especially where patent protection is believed by us to be of limited value. However, trade secrets and confidential know-how are difficult to protect, and we have limited control over the protection of trade secrets and confidential know-how used by our licensors, collaborators and suppliers. Because we have relied in the past on third parties to manufacture our product candidates, because we may continue to do so in the future, and because we expect to collaborate with third parties on the development of our current product candidates and any future product candidates we develop, we may, at times, share trade secrets with them. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Under such circumstances, trade secrets and confidential know-how can be difficult to maintain as confidential.

To protect this type of information against disclosure or appropriation by competitors, our policy is to require our employees, consultants, contractors and advisors to enter into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with us prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. However, current or former employees, consultants, contractors and advisers may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. The need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our competitive position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have an adverse effect on our business and results of operations. Enforcing a claim that a third party obtained illegally and is using trade secrets and/or confidential know-how is expensive, time consuming and unpredictable, and the enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. Courts outside the United States are sometimes less willing to protect proprietary information, technology and know-how.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

***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 trademark MeiraGTx has been registered in the EU and U.S. 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 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.

***We may need to license additional intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.***

The growth of our business may depend in part on our ability to acquire or in-license additional proprietary rights. For example, our programs may involve product candidates that may require the use of additional proprietary rights held by third parties. Our product candidates may also require specific formulations to work effectively and efficiently. These formulations may be covered by intellectual property rights held by others. We may develop products containing our compositions and pre-existing pharmaceutical compositions. These pharmaceutical products may be covered by intellectual property rights held by others. We may be required by the FDA, EMA or other foreign regulatory authorities to provide a companion diagnostic test or tests with our product candidates. These diagnostic test or tests 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. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license under such intellectual property rights, any such license may be non-exclusive, which may allow our competitors access to the same technologies licensed to us.

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

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. Although we seek to protect our ownership of intellectual property rights by ensuring that our agreements with our employees, collaborators and other third parties with whom we do business include provisions requiring such parties to assign rights in inventions to us, 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 our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and 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. Even if we are successful, litigation could result in substantial cost and reputational loss and be a distraction to our management and other employees.

#### **Risks Related to Employee Matters and Managing Growth**

***We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.***

As of September 30, 2018, we had 63 full-time employees. We will need to significantly expand our organization, and we may have difficulty identifying, hiring and integrating new personnel. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to

commercialize our product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our potential ability to generate revenue could be reduced and we may not be able to implement our business strategy. Many of the biotechnology companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles and a longer history in the industry than we do. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can discover and develop product candidates and operate our business will be limited.

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

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Alexandria Forbes, Ph.D., our President and Chief Executive Officer, Rich Giroux, our Chief Operating Officer and Stuart Naylor, Ph.D., our Chief Development Officer, as well as the other principal members of our management, scientific and clinical teams. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time and, for certain of our executive officers, entitle them to receive severance payments in connection with their voluntary resignation of employment.

If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. 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 develop, gain regulatory approval of and commercialize product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

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

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and significant negative media attention;
- withdrawal of participants from our clinical trials;
- significant costs to defend the related litigation and related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize our product candidates;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- decreased demand for our product candidates, if approved for commercial sale; and
- loss of revenue.

***Our insurance policies are expensive and protect us only from some business risks, which leaves us exposed to significant uninsured liabilities.***

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, clinical trial liability, employment practices liability, property, auto, workers' compensation, umbrella, cyber and directors' and officers' insurance.

Any additional product liability insurance coverage we acquire in the future, may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for our product candidates, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the commercialization of any product candidates we develop. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

We also expect that operating as a public company will make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers. We do not know, however, if we will be able to maintain existing insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash position and results of operations.

***Our employees and independent contractors, including consultants, vendors, and any third parties we may engage in connection with development and commercialization may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could harm our business.***

Misconduct by our employees and independent contractors, including consultants, vendors, and any third parties we may engage in connection with development and commercialization, could include intentional, reckless or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, EMA and other similar regulatory authorities, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud and abuse and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, 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 such 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 and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

***Our business and operations would suffer in the event of system failures.***

Our computer systems, as well as those of our contractors and consultants, are vulnerable to damage from computer viruses, unauthorized access, natural disasters (including hurricanes), terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product candidate development programs. For example, the loss of preclinical study or clinical trial data from completed, ongoing or planned 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 personal, confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, clinical trial data, proprietary business information, personal data and personally identifiable information of our clinical trial subjects and employees, in our data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors, or breached due to employee error, a technical vulnerability, malfeasance or other disruptions. Although, to our knowledge, we have not experienced any such material security breach to date, any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, significant regulatory penalties, and such an event could disrupt our operations, damage our reputation, and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay clinical development of our product candidates.

***We may engage in acquisitions that could disrupt our business, cause dilution to our shareholders or reduce our financial resources.***

In the future, we may enter into transactions to acquire other businesses, products or technologies. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our Ordinary Shares or other equity securities to the shareholders of the acquired company, which would reduce the percentage ownership of our existing shareholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and nondisruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

***The United Kingdom's withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business, which could reduce the price of our shares.***

Following the vote of a majority of the eligible members of the electorate in the United Kingdom to withdraw from the European Union in a national referendum held on June 23, 2016, the U.K. government served notice under Article 50 of the Treaty of the European Union on March 29, 2017 to formally initiate a withdrawal process. The United Kingdom and the European Union have a two-year period under Article 50 to negotiate the terms for withdrawal. Any extension of the negotiation period for withdrawal will require the consent of all of the remaining 27 member states. The referendum and withdrawal have created significant uncertainty about the future relationship between the United Kingdom and the European Union. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which EU-derived laws and regulations to replace or replicate as part of a withdrawal, including healthcare and pharmaceutical regulations; financial laws and regulations; tax and free trade agreements; intellectual property rights; supply chain logistics; environmental, health, and safety laws and regulations; immigration laws; and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs, depress economic activity, and restrict our access to capital. If the United Kingdom and the European Union are unable to negotiate acceptable withdrawal terms or if other EU member states pursue withdrawal, barrier-free access between the U.K. and other EU member states or among the European economic area overall could be diminished or eliminated. These developments, or the perception that any of them could occur, have had and may continue to have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Asset valuations, currency exchange rates, and credit ratings may be especially subject to increased market volatility. In addition, changes to U.K. border and immigration policy could occur as a result of the United Kingdom's withdrawal from the European Union, affecting our ability to recruit and retain employees from outside the United Kingdom. Any of these factors could have an adverse effect on our business, financial condition, results of operations, and prospects.

Further, the vote for the United Kingdom's withdrawal from the European Union has resulted in a decision to move the EMA from the United Kingdom to the Netherlands, with operations currently scheduled to begin in the Netherlands by end of March 2019. This transition may cause disruption in the administrative and medical scientific links between the EMA and the UK Medicines and Healthcare products Regulatory Agency, or the MHRA, including delays in granting clinical trial authorization or marketing authorization, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supply chain for clinical trial product and final authorized formulations. The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorization and commercialization of products in the European Union and/or the United Kingdom.

***Exchange rate fluctuations may adversely affect our results of operations and financial condition.***

Owing to the international scope of our operations, fluctuations in exchange rates, particularly between the pound sterling and the U.S. dollar, may adversely affect us. Although some of our operations are based in the United Kingdom, we source research and development, manufacturing, consulting and other services from the United States and the European Union. Further, potential future revenue may be derived from abroad, particularly from the United States. As a result, our business and the market price of our securities may be affected by fluctuations in foreign exchange rates not only between the pound sterling and the U.S. dollar, but also the euro, which may have a significant impact on our results of operations and cash flows from period to period. Currently, we do not have any exchange rate hedging arrangements in place.

**Risks Related to Our Ordinary Shares**

***The market price of our ordinary shares may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our ordinary shares.***

Our share price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your ordinary shares at or above your purchase price. The market price for our ordinary shares may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or expected changes in our growth rate relative to our competitors;
- results of clinical trials of our product candidates or those of our competitors;
- developments related to our existing or any future collaborations;
- regulatory or legal developments in the United States and other countries;
- development of new product candidates that may address our markets and make our product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less useful;
- announcements by us, our partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or expected changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions;

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- changes in accounting principles; and
- the other factors described in this “Risk Factors” section and elsewhere in this Quarterly Report on Form 10-Q.

In addition, the stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, when the market price of a security has been volatile, holders of that security have sometimes instituted securities class action litigation against the issuer. If any of the holders of our ordinary shares were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our senior management would be diverted from the operation of our business. Any adverse determination in litigation could also subject us to significant liabilities. Broad market and industry factors may negatively affect the market price of our ordinary shares, regardless of our actual operating performance. Further, a decline in the financial markets and related factors beyond our control may cause the price of our ordinary shares to decline rapidly and unexpectedly. If the market price of our ordinary shares does not exceed your purchase price, you may not realize any return on your investment in us and may lose some or all of your investment.

***Our executive officers, directors and principal shareholders, if they choose to act together, have the ability to control or significantly influence all matters submitted to shareholders for approval.***

As of September 30, 2018, our executive officers, directors and shareholders who owned more than 5% of our outstanding ordinary shares and their respective affiliates, in the aggregate, hold ordinary shares representing approximately 56.0% of our outstanding ordinary shares.

As a result, if these shareholders choose to act together, they would be able to control or significantly influence all matters submitted to our shareholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors, the composition of our management and approval of any merger, consolidation, sale of all or substantially all of our assets or other business combination that other shareholders may desire. Any of these actions could adversely affect the market price of our ordinary shares.

***A significant portion of our total outstanding shares are eligible to be sold into the market in the near future, which could cause the market price of our ordinary shares to drop significantly, even if our business is doing well.***

Sales of a substantial number of our ordinary shares in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our ordinary shares. Substantially all of our 27,184,132 Ordinary Shares are or will become eligible to be sold within 6 months of our IPO. Moreover, holders of an aggregate of 16,059,333 ordinary shares will have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other shareholders, until such shares can otherwise be sold without restriction under Rule 144 or until the rights terminate pursuant to the terms of the shareholders agreement between us and such holders. We have also registered 4,669,342 ordinary shares subject to equity awards issued or reserved for future issuance under our equity compensation plans on a registration statement on Form S-8. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and lock-up agreements. Any sales of securities by these shareholders could have a negative impact on the trading price of our ordinary shares.

***We are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies may make our ordinary shares less attractive to investors.***

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of our IPO. However, if certain events occur prior to the end of such five-year period, including if we become a “large accelerated filer,” our annual gross revenues exceed \$1.07 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure in this Quarterly Report on Form 10-Q;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;

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- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We cannot predict whether investors will find our ordinary shares less attractive if we rely on these exemptions. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and our share price may be reduced or more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have elected to take advantage of this extended transition period.

### ***We will incur increased costs as a result of operating as a public company, and our management will be 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, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the Nasdaq listing requirements 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 will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be 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 will be 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, 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 whether such controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. 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 reports about our business, or if they issue an adverse or misleading opinion regarding our ordinary shares, our share price and trading volume could decline.***

The trading market for our ordinary shares relies in part on the research and reports that industry or securities analysts publish about us or our business. We do not control these analysts. Furthermore, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our share performance, or if any of our preclinical studies or clinical trials and operating results fail to meet the expectations of analysts, our share price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our share price or trading volume to decline.

***Anti-takeover provisions in our organizational documents and Cayman Islands law may discourage or prevent a change of control, even if an acquisition would be beneficial to our shareholders, which could depress the price of our ordinary shares and prevent attempts by our shareholders to replace or remove our current management.***

Our memorandum and articles of association contain provisions that may discourage unsolicited takeover proposals that shareholders may consider to be in their best interests. Our board of directors is divided into three classes with staggered, three year terms. Our board of directors has the ability to designate the terms of and issue preferred shares without shareholder approval. We are also subject to certain provisions under Cayman Islands law that could delay or prevent a change of control. Together these provisions may make more difficult the removal of management and may discourage transactions that otherwise could involve payment of a premium over prevailing market prices for our ordinary shares.

***There may be difficulties in enforcing foreign judgments against our management or us.***

Certain of our directors and management reside outside the United States. A significant portion of our assets and such persons' assets are located outside the United States. As a result, it may be difficult or impossible for investors to effect service of process upon us within the United States or other jurisdictions, including judgments predicated upon the civil liability provisions of the federal securities laws of the United States. In particular, investors should be aware that there is uncertainty as to whether the courts of the Cayman Islands or any other applicable jurisdictions would recognize and enforce judgments of U.S. courts obtained against us or our directors or management as well as against the selling shareholders predicated upon the civil liability provisions of the securities laws of the United States or any state in the United States or entertain original actions brought in the Cayman Islands or any other applicable jurisdictions courts against us or our directors or officers as well as against the selling shareholders predicated upon the securities laws of the United States or any state in the United States.

***The rights of our shareholders differ from the rights typically offered to shareholders of a U.S. corporation.***

Our corporate affairs and the rights of holders of ordinary shares are governed by Cayman Islands law, including the provisions of the Cayman Islands Companies Law (2018 Revision), or the Companies Law, the common law of the Cayman Islands and by our memorandum and articles of association. We will also be subject to the federal securities laws of the United States. The rights of shareholders to take action against the directors, actions by minority shareholders and the fiduciary responsibilities of our directors to us under Cayman Islands law are to a large extent governed by the common law of the Cayman Islands. The common law of the Cayman Islands is derived in part from comparatively limited judicial precedent in the Cayman Islands as well as from English common law, the decisions of whose courts are of persuasive authority, but are not binding on a court in the Cayman Islands. The rights of our shareholders and the fiduciary responsibilities of our directors under Cayman Islands law are different from what they would be under statutes or judicial precedent in some jurisdictions in the United States. In particular, the Cayman Islands has a different body of securities laws as compared to the United States, and certain states, such as Delaware, may have more fully developed and judicially interpreted bodies of corporate law. In addition, Cayman Islands companies may not have standing to initiate a shareholders derivative action in a Federal court of the United States. As a result of all of the above, public shareholders may have more difficulty in protecting their interests in the face of actions taken by management, members of the board of directors or controlling shareholders than they would as public shareholders of a United States company.

***If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our ordinary shares.***

Section 404(a) of the Sarbanes-Oxley Act, or Section 404(a), requires that beginning with our second annual report following our initial public offering on June 7, 2018, management assess and report annually on the effectiveness of our internal control over financial reporting and identify any material weaknesses in our internal control over financial reporting. Although Section 404(b) of the Sarbanes-Oxley Act, or Section 404(b), requires our independent registered public accounting firm to issue an annual report that addresses the effectiveness of our internal control over financial reporting, we have opted to rely on the exemptions provided in the JOBS Act, and consequently will not be required to comply with SEC rules that implement Section 404(b) until such time as we are no longer an "emerging growth company."

We expect our first Section 404(a) assessment will take place for our annual report for the fiscal year ending December 31, 2019. Effective internal controls over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inadequate internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our ordinary shares.

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

Under current Cayman Islands law, the company may only make distributions by way of dividend out of profits, or out of its share premium account (provided that immediately following the date that the dividend is proposed to be paid the company is able to pay its debts as they fall due in the ordinary course of business). We have never declared or paid any cash dividends on our ordinary shares. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our ordinary shares would be your sole source of gain on an investment in our ordinary shares for the foreseeable future.

***We could be subject to securities class action litigation.***

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 biopharmaceutical companies have experienced significant stock price volatility in recent years. 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.

***We expect to be treated as resident in the United Kingdom for tax purposes, but may be treated as a dual resident company for United Kingdom tax purposes.***

It is the intention of our board of directors to conduct our affairs so that the central management and control of the company is exercised in the United Kingdom. As a result, we expect to be treated as resident in the United Kingdom for UK tax purposes. Accordingly, we expect to be subject to UK taxation on our income and gains, except where an exemption applies.

However, we may be treated as a dual resident company for UK tax purposes. As a result, our right to claim certain reliefs from UK tax may be restricted, and changes in law or practice in the United Kingdom could result in the imposition of further restrictions on our right to claim UK tax reliefs.

***We may be classified as a passive foreign investment company for U.S. federal income tax purposes, which could result in adverse U.S. federal income tax consequences to U.S. investors in our ordinary shares.***

Based on the current and anticipated value of our assets, including goodwill, and the composition of our income, assets and operations, we do not believe we were a "passive foreign investment company," or PFIC, for the taxable year ending on December 31, 2017, and do not expect to be a PFIC for the current taxable year. However, the application of the PFIC rules is subject to uncertainty in several respects, and we cannot assure you that the U.S. Internal Revenue Service, or the IRS, will not take a contrary position. Furthermore, a separate determination must be made after the close of each taxable year as to whether we are a PFIC for that year. Accordingly, we cannot assure you that we were not a PFIC for our taxable year ending on December 31, 2017 and that we will not be a PFIC for our current taxable year or any future taxable year. A non-U.S. company will be considered a PFIC for any taxable year if (i) at least 75% of its gross income is passive income (including interest income), or (ii) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during a taxable year) is attributable to assets that produce or are held for the production of passive income. If we were to be classified as a PFIC for any taxable year during which a U.S. Holder (as defined below under "Material U.S. Federal Income Tax Consequences") holds our ordinary shares, certain adverse U.S. federal income tax consequences could apply to such U.S. Holder, including (i) the treatment of all or a portion of any gain on disposition of our ordinary shares as ordinary income, (ii) the application of a deferred interest charge on such gain and the receipt of certain dividends and (iii) the obligation to comply with certain reporting requirements.

***If a United States person is treated as owning at least 10% of our ordinary shares, such holder may be subject to adverse U.S. federal income tax consequences.***

If a U.S. Holder is treated as owning (directly, indirectly or constructively) at least 10% of the value or voting power of our ordinary shares, such U.S. Holder may be treated as a “United States shareholder” with respect to each “controlled foreign corporation” in our group (if any). If our group includes one or more U.S. subsidiaries, certain of our non-U.S. subsidiaries could be treated as controlled foreign corporations (regardless of whether we are treated as a controlled foreign corporation). A United States shareholder of a controlled foreign corporation may be required to report annually and include in its U.S. taxable income its pro rata share of “Subpart F income,” “global intangible low-taxed income” and investments in U.S. property by controlled foreign corporations, regardless of whether we make any distributions. An individual that is a United States shareholder with respect to a controlled foreign corporation generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a United States shareholder that is a U.S. corporation. Failure to comply with these reporting obligations may subject you to significant monetary penalties and may prevent the statute of limitations from starting with respect to your U.S. federal income tax return for the year for which reporting was due. We cannot provide any assurances that we will assist investors in determining whether any of our non-U.S. subsidiaries is treated as a controlled foreign corporation or whether such investor is treated as a United States shareholder with respect to any of such controlled foreign corporations. Further, we cannot provide any assurances that we will furnish to any United States shareholders information that may be necessary to comply with the aforementioned reporting and tax payment obligations. U.S. Holders should consult their tax advisors regarding the potential application of these rules to their investment in our ordinary shares.

***Comprehensive tax reform legislation could adversely affect our business and financial condition.***

The U.S. government has recently enacted comprehensive tax legislation that includes significant changes to the taxation of business entities, referenced herein as the Tax Reform Act. These changes include, among others, a permanent reduction to the corporate income tax rate, limiting interest deductions and the use of net operating losses, adopting elements of a territorial tax system and introducing certain anti-base erosion provisions. We continue to examine the impact this tax reform legislation may have on our business. The effect of the Tax Reform Act on our business, whether adverse or favorable, is uncertain, and may not become evident for some period of time. U.S. Holders should consult their legal and tax advisors regarding any such legislation and the potential tax consequences of investing in our ordinary shares.

***Changes in tax laws or challenges to our tax position could adversely affect our results of operations and financial condition.***

We are subject to complex tax laws. Changes in tax laws, regulations and treaties, or the interpretation thereof, tax policy initiatives and reforms under consideration and the practices of tax authorities in jurisdictions in which we operate could adversely affect our tax position, including our effective tax rate or tax payments.

In October 2015, the Organization for Economic Co-Operation and Development released a final package of measures to be implemented by member nations in response to a 2013 action plan calling for a coordinated multi-jurisdictional approach to “base erosion and profit shifting” by multinational companies. Multiple member jurisdictions, including the countries in which we operate, have begun implementing recommended changes such as country-by-country reporting requirements and changes to double tax treaties. Additional multilateral changes are anticipated in upcoming years. We often rely on generally available interpretations of applicable tax laws, treaties and regulations. There cannot be certainty that the relevant tax authorities are in agreement with our interpretation of these laws, regulations or treaties, or with tax positions that we have taken. If our interpretation or tax position is challenged by the relevant tax authorities, we could be required to pay taxes that we currently do not collect or pay, may be subject to interest and penalties and there could be an increase to the costs of our services to track and collect such taxes, which could increase our costs of operations or our effective tax rate. Similarly, a tax authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a “permanent establishment” under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. The occurrence of any of the foregoing tax risks could have a material adverse effect on our business, financial condition and results of operations.

We are unable to predict what national or international tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could impact the tax treatment of our earnings, adversely affect our profitability and increase the complexity, burden and cost of tax compliance.

*We have significant net operating losses, or NOLs, and U.K. carryforward tax losses which we may not be able to realize or which may be restricted following the Corporate Reorganization or any future change of control. We also benefit from certain tax incentive regimes, such as research and development tax credits, in the jurisdictions in which we operate and any adverse change to these regimes, the application thereof or challenges to the tax position we have adopted under these regimes could adversely affect our results of operations and financial condition.*

As of September 30, 2018, we had federal and state NOL carryforwards in the United States of \$12.4 million and \$12.4 million, respectively, and cumulative carryforward tax losses in the United Kingdom of \$96.4 million, which we expect to be available to reduce future taxable income subject to any relevant restrictions (including those in the UK that limit the percentage of profits that can be reduced by carried forward losses). The U.S. federal and state NOL carry forwards will begin to expire in 2035 and the U.K. carryforward tax losses will continue indefinitely, subject to relevant restrictions, under current UK legislation. Also, as of September 30, 2018, we had orphan drug and research and development credits in the U.S. in the amount of \$0.2 million and \$0.5 million, respectively.

The NOL carry forwards and U.K. carryforward tax losses are subject to review and possible adjustment by the U.S., U.K. and state tax authorities. NOL carryforwards and U.K. carryforward tax losses may become subject to limitations in the event of certain cumulative changes in the ownership interest of significant shareholders, as defined under Sections 382 Internal Revenue Code, as well as the Corporation Tax Act 2010 Part 14 under the UK tax rules. This could limit the amount of NOLs or carryforward tax losses that we can utilize annually to offset future taxable income or tax liabilities. Subsequent ownership changes and changes to the UK (or US) tax rules in respect of the utilization of losses carried forward may further affect the limitation in future years.

Additionally, we have not undertaken a study on the completeness of the U.S. research and development credit. As such, the U.S. research and development credits may change and may be subject to review and adjustment by the tax authorities.

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

On June 12, 2018, we completed our IPO and issued and sold 5,000,000 ordinary shares at a price to the public of \$15.00 per share receiving \$65.3 million in proceeds after deducting underwriting discounts and commissions and offering expenses payable by us. There has been no material change in the expected use of the net proceeds from our IPO as described in our Prospectus. As of September 30, 2018, we had used \$13.5 million of such net proceeds and had total unrestricted cash and cash equivalents of \$88.6 million.

**Item 3. Defaults Upon Senior Securities.**

None

**Item 4. Mine Safety Disclosures.**

Not applicable.

**Item 5. Other Information.**

None

## Table of Contents

### Item 6. Exhibits.

<u>Exhibit Number</u>	<u>Description</u>
3.1	<a href="#">Memorandum and Articles of Association of the Registrant, dated June 7, 2018 (incorporated by reference to Exhibit 3.3 of the Company's Registration Statement on Form S-1 (File No. 333-224914) filed on June 4, 2018).</a>
31.1*	<a href="#">Rule 13a-14(a) and 15d-14(a) Certification of Principal Executive Officer.</a>
31.2*	<a href="#">Rule 13a-14(a) and 15d-14(a) Certification of Principal Financial Officer.</a>
32.1**	<a href="#">Section 1350 Certification of Principal Executive Officer.</a>
32.2**	<a href="#">Section 1350 Certification of Principal Financial Officer.</a>
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

\* Filed herewith.

\*\* Furnished herewith.

**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.

Company Name

Date: November 8, 2018

By: \_\_\_\_\_  
/s/ Alexandria Forbes  
**Alexandria Forbes**  
**Chief Executive Officer**

Date: November 8, 2018

By: \_\_\_\_\_  
/s/ Katherine Breedis  
**Katherine Breedis**  
**Chief Financial Officer (principal financial officer and  
principal accounting officer)**

## CERTIFICATION

I, Alexandria Forbes, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of MeiraGTx Holdings plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
  - o Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - o [Omitted];
  - o Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - o Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - o All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - o Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 8, 2018

By: \_\_\_\_\_  
/s/ Alexandria Forbes  
**Alexandria Forbes**  
**Chief Executive Officer**

## CERTIFICATION

I, Katherine Breedis, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of MeiraGTx Holdings plc;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) [Omitted];
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 8, 2018

By: \_\_\_\_\_ /s/ Katherine Breedis  
**Katherine Breedis**  
**Chief Financial Officer (principal financial officer)**

**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Quarterly Report of MeiraGTx Holdings plc (the "Company") on Form 10-Q for the period ending September 30, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: November 8, 2018

By: \_\_\_\_\_ /s/ Alexandria Forbes

**Alexandria Forbes**  
**Chief Executive Officer**

**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Quarterly Report of MeiraGTx Holdings plc (the "Company") on Form 10-Q for the period ending September 30, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: November 8, 2018

By: \_\_\_\_\_ /s/ Katherine Breedis  
**Katherine Breedis**  
**Chief Financial Officer (principal financial officer)**