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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 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, 2019

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.)

450 East 29th Street, 15th Floor  
New York, NY  
(Address of principal executive offices)

10016  
(Zip Code)

Registrant's telephone number, including area code: (646) 860-7985  
Not Applicable  
(Former name, former address, and former fiscal year, if changed since last report)

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**Securities registered pursuant to Section 12(b) of the Act:**

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary Shares, \$0.00003881 par value per share	MGTX	The Nasdaq Global Select Market

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, anon-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, 2019, the registrant had 36,571,722 ordinary shares, \$0.00003881 par value per share, outstanding.

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### **Forward-Looking Statements**

This Quarterly Report on Form 10-Q (the “Form 10-Q”) contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this Form 10-Q that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding expectations regarding meetings with global regulatory authorities and the FDA, product pipeline, anticipated product benefits, goals and strategic priorities, product candidate development and status and expectations relating to clinical trials, growth expectations or targets and pre-clinical and clinical data expectations in respect of collaborations, 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 Form 10-Q. These and other important factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this Form 10-Q. Any such forward-looking statements represent management’s estimates as of the date of this Form 10-Q. 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 Form 10-Q.

### **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 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>2019</u>	<u>December 31,</u> <u>2018</u>
	<u>(unaudited)</u>	
<b>ASSETS</b>		
<b>CURRENT ASSETS:</b>		
Cash and cash equivalents	\$ 253,330,623	\$ 68,080,175
Prepaid expenses	6,248,981	1,937,785
Other current assets	<u>11,509,144</u>	<u>4,634,105</u>
Total Current Assets	271,088,748	74,652,065
Right-of-use assets	28,801,757	—
Property and equipment, net	16,899,147	22,014,237
Security deposits	839,149	105,085
Restricted cash	<u>123,376</u>	<u>123,376</u>
<b>TOTAL ASSETS</b>	<b><u>\$ 317,752,177</u></b>	<b><u>\$ 96,894,763</u></b>
<b>LIABILITIES AND SHAREHOLDERS' EQUITY</b>		
<b>CURRENT LIABILITIES:</b>		
Accounts payable	\$ 3,798,441	\$ 3,042,861
Accrued expenses	9,346,895	11,991,697
Lease obligations, current	2,028,689	27,199
Deferred revenue - related party, current	24,115,777	—
Other current liabilities	<u>—</u>	<u>437,053</u>
Total Current Liabilities	39,289,802	15,498,810
Deferred revenue - related party	62,837,715	—
Lease obligations	20,600,077	7,097
Deferred rent	—	201,264
Asset retirement obligations	<u>131,213</u>	<u>128,119</u>
<b>TOTAL LIABILITIES</b>	<b><u>122,858,807</u></b>	<b><u>15,835,290</u></b>
<b>COMMITMENTS</b>		
<b>SHAREHOLDERS' EQUITY:</b>		
Ordinary Shares, \$0.00003881 par value, 1,288,327,750 authorized 36,571,722 issued and outstanding at September 30, 2019 27,386,632 issued and outstanding at December 31, 2018	1,420	1,064
Capital in excess of par value	390,053,479	229,054,460
Accumulated other comprehensive income	2,393,372	293,666
Accumulated deficit	<u>(197,554,901)</u>	<u>(148,289,717)</u>
Total Shareholders' Equity	<u>194,893,370</u>	<u>81,059,473</u>
<b>TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY</b>	<b><u>\$ 317,752,177</u></b>	<b><u>\$ 96,894,763</u></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,		For the Nine-Month Period Ended September 30,	
	2019	2018	2019	2018
License revenue - related party	\$ 3,582,586	\$ —	\$ 6,349,222	\$ —
Operating expenses:				
General and administrative	\$ 9,874,810	\$ 6,629,052	\$ 31,811,456	\$ 35,129,120
Research and development	4,614,446	8,109,160	27,362,432	22,827,176
Total operating expenses	14,489,256	14,738,212	59,173,888	57,956,296
Loss from operations	(10,906,670)	(14,738,212)	(52,824,666)	(57,956,296)
Other non-operating income (expense):				
Foreign currency gain (loss)	115,470	(677,488)	3,117,047	(2,425,488)
Change in fair value of warrant liability	—	—	—	(1,514,775)
Other income	—	—	—	83,075
Interest income	959	264	40,686	50,926
Interest expense	(9,283)	(9,508)	(28,311)	(46,571)
Loss before income taxes	(10,799,524)	(15,424,944)	(49,695,244)	(61,809,129)
Benefit for income taxes	338,670	—	430,060	—
Net loss	(10,460,854)	(15,424,944)	(49,265,184)	(61,809,129)
Other comprehensive income:				
Foreign currency translation, net of tax of \$338,670 and \$0 for the three-month periods ended September 30, 2019 and 2018, respectively and \$430,060 and \$0 for the nine-month periods ended September 30, 2019 and 2018, respectively	1,653,507	508,758	2,099,706	1,730,000
Total comprehensive loss	\$ (8,807,347)	\$ (14,916,186)	\$ (47,165,478)	\$ (60,079,129)
Net loss	\$ (10,460,854)	\$ (15,424,944)	\$ (49,265,184)	\$ (61,809,129)
Accretion on convertible preferred C shares and warrants	—	—	—	(1,806,512)
Adjusted net loss	\$ (10,460,854)	\$ (15,424,944)	\$ (49,265,184)	\$ (63,615,641)
Basic and diluted adjusted net loss per ordinary share	\$ (0.30)	\$ (0.59)	\$ (1.53)	\$ (3.89)
Weighted-average number of ordinary shares outstanding	34,663,623	26,340,450	32,111,733	16,355,849

See Notes to Condensed Consolidated Financial Statements

**MEIRAGTX HOLDINGS PLC AND SUBSIDIARIES**  
**CONDENSED CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY**  
**AS OF SEPTEMBER 30, 2019**  
**(unaudited)**

	Ordinary Shares	Amount	Capital in Excess of Par Value	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Shareholders' Equity
Balance at December 31, 2018	27,386,632	\$1,064	\$ 229,054,460	\$ 293,666	\$(148,289,717)	\$ 81,059,473
Issuance of ordinary shares in connection with a license agreement	158,832	6	1,966,334	—	—	1,966,340
Sale of ordinary shares in connection with private placement, net of issuance costs of \$2,426,953	5,797,102	225	77,572,822	—	—	77,573,047
Share-based compensation	—	—	2,934,991	—	—	2,934,991
Foreign currency translation	—	—	—	(1,133,683)	—	(1,133,683)
Net loss for the three-month period ended March 31, 2019	—	—	—	—	(17,981,918)	(17,981,918)
Balance at March 31, 2019	33,342,566	\$1,295	\$ 311,528,607	\$ (840,017)	\$(166,271,635)	\$144,418,250
Exercise of share options	225	—	1,267	—	—	1,267
Share-based compensation	—	—	4,386,123	—	—	4,386,123
Foreign currency translation, net of income taxes	—	—	—	1,579,882	—	1,579,882
Net loss for the three-month period ended June 30, 2019	—	—	—	—	(20,822,412)	(20,822,412)
Balance at June 30, 2019	33,342,791	\$1,295	\$ 315,915,997	\$ 739,865	\$(187,094,047)	\$129,563,110
Sale of ordinary shares in connection with public offering, net of issuance costs of \$5,042,795	3,200,000	124	70,157,088	—	—	70,157,212
Issuance of ordinary shares in connection with payables	19,807	1	421,499	—	—	421,500
Exercise of share options	9,124	—	53,344	—	—	53,344
Share-based compensation	—	—	3,505,551	—	—	3,505,551
Foreign currency translation, net of income taxes of \$338,670	—	—	—	1,653,507	—	1,653,507
Net loss for the three-month period ended September 30, 2019	—	—	—	—	(10,460,854)	(10,460,854)
Balance at September 30, 2019	<u>36,571,722</u>	<u>\$1,420</u>	<u>390,053,479</u>	<u>2,393,372</u>	<u>(197,554,901)</u>	<u>194,893,370</u>

See Notes to Condensed Consolidated Financial Statements

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

	Convertible Preferred C Shares		Shareholders' (Deficit) Equity					
	Convertible Preferred C Shares	Amount	A Ordinary Shares	Amount	Capital in Excess of Par Value	Accumulated Other Comprehensive (Loss)	Accumulated Deficit	Shareholders' (Deficit) Equity
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	4,212,453	43,851,602	—	—	—	—	—	—
Accretion of issuance costs on convertible preferred C shares	—	94,445	—	—	(94,445)	—	—	(94,445)
Accretion of warrants issued in connection with convertible preferred C shares	—	570,273	—	—	(570,273)	—	—	(570,273)
Share-based compensation	—	—	550,162	22	4,275,713	—	—	4,275,735
Foreign currency translation	—	—	—	—	—	(757,765)	—	(757,765)
Net loss for the three-month period ended March 31, 2018	—	—	—	—	—	—	(16,403,353)	(16,403,353)
Balance at March 31, 2018	9,361,167	\$ 97,351,080	9,376,352	\$ 364	\$ 23,691,708	\$ (2,780,242)	\$ (81,827,196)	\$ (60,915,366)
Sale of convertible preferred C shares, net of issuance costs	1,212,671	\$ 12,307,517	—	—	—	—	—	—
Accretion of issuance costs on convertible preferred C shares	—	666,567	—	—	(666,567)	—	—	(666,567)
Accretion of warrants issued in connection with convertible preferred C shares	—	475,227	—	—	(475,227)	—	—	(475,227)
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 ordinary shares in initial public offering, net of issuance costs of \$9,541,530	—	—	5,000,000	194	65,458,276	—	—	65,458,470
Share-based compensation	—	—	1,306,348	51	8,357,770	—	—	8,357,821
Foreign currency translation	—	—	—	—	—	1,979,007	—	1,979,007
Net loss for the three-month period ended June 30, 2018	—	—	—	—	—	—	(29,980,832)	(29,980,832)
Balance at June 30, 2018	—	\$ —	27,184,132	\$ 1,055	\$ 221,080,313	\$ (801,235)	\$ (111,808,028)	\$ 108,472,105
Additional issuance costs in connection with A ordinary shares issued in June 2018	—	—	—	—	(134,205)	—	—	(134,205)
Share-based compensation	—	—	—	—	2,922,357	—	—	2,922,357
Foreign currency translation	—	—	—	—	—	508,758	—	508,758
Net loss for the three-month period ended September 30, 2018	—	—	—	—	—	—	(15,424,944)	(15,424,944)
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**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**  
**(unaudited)**

For the Nine-Month Period Ended September 30,  
2019                      2018

	2019	2018
<b>Cash flows from operating activities:</b>		
Net loss	\$ (49,265,184)	\$ (61,809,129)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Ordinary shares issued in connection with license agreements	1,966,340	137,658
Share-based compensation expense	10,826,665	15,555,913
Foreign currency (gain) loss	(3,117,047)	2,425,488
Depreciation	1,569,098	1,549,686
Amortization of interest on asset retirement obligation	7,861	10,918
Change in fair value of warrant liability	—	1,514,775
Benefit for income taxes	(430,060)	—
(Increase) decrease in operating assets:		
Prepaid expenses	(4,413,356)	(112,440)
Other current assets	(6,358,738)	239,627
Security deposits	(745,275)	(180,980)
Increase (decrease) in operating liabilities:		
Accounts payable	1,415,012	(2,337,302)
Accrued expenses	(2,428,405)	(3,496,882)
Other current liabilities	(436,161)	—
Due to Kadmon	—	(861,030)
Deferred revenue	93,120,824	—
Lease obligations	304,713	—
Deferred rent	—	(55,460)
<b>Net cash provided by (used in) operating activities</b>	<b>42,016,287</b>	<b>(47,419,158)</b>
<b>Cash flows from investing activities:</b>		
Purchase of property and equipment	(4,230,740)	(2,372,622)
<b>Net cash used in investing activities</b>	<b>(4,230,740)</b>	<b>(2,372,622)</b>
<b>Cash flows from financing activities:</b>		
Payments on lease obligations - financing leases	(17,923)	(23,772)
Exercise of warrants	—	9,720,000
Exercise of share options	54,611	—
Proceeds from the sale of ordinary shares	155,200,007	69,750,000
Issuance costs in connection with ordinary shares	(7,469,748)	(4,115,843)
Proceeds from the sale of convertible preferred C shares, net of issuance costs	—	56,849,594
Issuance costs in connection with convertible preferred C shares	—	(690,475)
Payment of note payable	—	(1,442,009)
<b>Net cash provided by financing activities</b>	<b>147,766,947</b>	<b>130,047,495</b>
Net increase in cash, cash equivalents and restricted cash	185,552,494	80,255,715
Effect of exchange rate changes on cash	(302,046)	(243,719)
Cash, cash equivalents and restricted cash at beginning of period	68,203,551	8,672,014
Cash, cash equivalents and restricted cash at end of period	<b>\$ 253,453,999</b>	<b>\$ 88,684,010</b>
<b>Supplemental disclosure of non-cash transactions:</b>		
Lease obligations for right-of-use asset	\$ 22,932,582	\$ —
Issuance of shares in connection with payables	\$ 421,500	\$ 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
Issuance costs in connection with sale of ordinary shares in accounts payable and accrued expenses at end of period	\$ —	\$ 309,892
<b>Supplemental disclosure of cash flow information:</b>		
Cash paid for interest	\$ 1,219	\$ 31,531

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 and subsidiaries (the “Company” or “Meira Holdings”), an exempted company incorporated 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 few or no effective treatments available. The Company is focused on developing therapies for ocular diseases, including inherited retinal diseases, as well as xerostomia following radiation treatment for head and neck cancers, and neurodegenerative diseases such as Parkinson’s disease (“PD”) and amyotrophic lateral sclerosis (“ALS”). The Company also owns and operates a current good manufacturing practices, or cGMP, multi-product, multi-viral vector manufacturing facility in London, United Kingdom, which includes fill and finish capabilities and can supply the Company’s clinical and potential commercial material.

*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 GAAP 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, 2019 are not necessarily indicative of the final results that may be expected for the year ended December 31, 2019. These unaudited condensed consolidated financial statements should be read in conjunction with the audited consolidated financial statements and the notes thereto for the year ended December 31, 2018 included in the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2018 (the “Form 10-K”).

*Liquidity*

The Company 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. The Company’s accumulated deficit at September 30, 2019 totaled \$197,554,901, and management expects to incur substantial 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. For the nine-months ended September 30, 2019, the Company generated \$42,016,287 of positive cash flows from operations. However, prior to the nine-months ended September 30, 2019, the Company did not generate positive cash flows from operations and there are no assurances that the Company will generate positive cash flows in the future. Additionally, 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, 2019, the Company had cash and cash equivalents in the amount of \$253,330,623, which consisted of depository accounts. On January 30, 2019, the Company entered into a collaboration, option and license agreement with Janssen Pharmaceuticals, Inc. (“Janssen”) one of the Janssen Pharmaceuticals Companies of Johnson & Johnson (the “Collaboration Agreement”). Under the terms of the Collaboration Agreement, the Company received an upfront payment of \$100,000,000. The Company will also receive funding for certain research, manufacturing, clinical development and commercialization costs, potential additional milestone payments upon the achievement of such milestones and royalties on future net sales of products. The Company estimates that its cash and cash equivalents on hand at September 30, 2019 will be sufficient to cover its expenses for at least the next twelve months from the date of issuance of these condensed consolidated financial statements.

***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 capital resources and operations to date have been funded primarily with the proceeds from the Collaboration Agreement, private and public 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, 2018 included in the Company's Form 10-K. 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;

MeiraGTx, LLC, a Delaware corporation;

MeiraGTx UK II Limited, a limited company under the laws of England and Wales ("Meira UK II");

BRI-Alzan, Inc., a Delaware corporation;

MeiraGTx B.V., a Netherlands corporation;

MeiraGTx Neurosciences, Inc., a Delaware corporation; and

MeiraGTx UK Limited, 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 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: collaboration revenue (as disclosed in Note 8), the accounting for research and development costs, warrants, share-based compensation, leases 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, 2019	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable (Level 3)
Restricted cash	\$ 123,376	\$ 123,376	\$ —	\$ —
Asset retirement obligations	\$ 131,213	\$ —	\$ —	\$ 131,213

Description	Fair Value Measurement Using:			
	December 31, 2018	Significant Observable Inputs (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable (Level 3)
Restricted cash	\$ 123,376	\$ 123,376	\$ —	\$ —
Asset retirement obligations	\$ 128,119	\$ —	\$ —	\$ 128,119

### **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 Obligations**

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 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.

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The change in asset retirement obligations is as follows:

	September 30, 2019	December 31, 2018
Balance at beginning of period	\$ 128,119	\$ 178,419
Additional asset retirement obligations during the period	—	69,286
Amortization of interest	7,861	(38,301)
Change in estimate	—	(99,090)
Effects of exchange rate	(4,767)	17,805
Balance at end of period	<u>\$ 131,213</u>	<u>\$ 128,119</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 for the drug product for the clinical studies and preclinical activities; facilities; supplies; rent, insurance, certain legal fees, share-based compensation, depreciation and other costs associated with clinical and preclinical activities and regulatory operations. Research funding under collaboration agreements is recorded as an offset to these costs.

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 consolidated financial statements as prepaid expenses or accrued expenses, as the case may be.

### **Collaboration Arrangements**

The Company evaluates its collaborative arrangements pursuant to ASC 808, *Collaborative Arrangements* ("ASC 808") and ASC 606, *Revenue from Contracts with Customers* ("ASC 606"). The Company considers the nature and contractual terms of collaborative arrangements and assesses whether the arrangement involves a joint operating activity pursuant to which the Company is an active participant and is exposed to significant risks and rewards with respect to the arrangement. If the Company is an active participant and is exposed to significant risks and rewards with respect to the arrangement, the Company accounts for the arrangement as a collaboration under ASC 808. To date, the Company has entered into two separate collaboration agreements, both of which are with Janssen, which were determined to be within the scope of ASC 808.

ASC 808 does not address recognition or measurement matters related to collaborative arrangements. Payments between participants pursuant to a collaborative arrangement that are within the scope of other authoritative accounting literature on income statement classification are accounted for using the relevant provisions of that literature. If the payments are not within the scope of other authoritative accounting literature, the income statement classification for the payments is based on an analogy to authoritative accounting literature or if there is no appropriate analogy, a reasonable, rational and consistently applied accounting policy election. Payments received from a collaboration partner to which this policy applies may include upfront payments in respect of a license of intellectual property, development and commercialization-based milestones, and royalties.

Refer to the discussion in Note 8 for further information related to the accounting for the Janssen Collaboration Agreement.

### **Revenue Recognition**

Arrangements with collaborators may include licenses to intellectual property, research and development services, manufacturing services for clinical and commercial supply, and participation on joint steering committees. The Company evaluates the promised goods or services to determine which promises, or group of promises, represent performance obligations. In contemplation of whether a promised good or service meets the criteria required of a performance obligation, the Company considers the stage of development of the underlying intellectual property, the capabilities and expertise of the customer relative to the underlying intellectual property, and whether the promised goods or services are integral to or dependent on other promises in the contract. When accounting for an arrangement that contains multiple performance obligations, the Company must develop judgmental assumptions, which may include market conditions, reimbursement rates for personnel costs, development timelines and probabilities of regulatory success to determine the stand-alone selling price for each performance obligation identified in the contract.

When the Company concludes that a contract should be accounted for as a combined performance obligation and recognized over time, the Company must then determine the period over which revenue should be recognized and the method by which to measure revenue. The Company generally recognizes revenue using a cost-based input method.

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The Collaboration Agreement with Janssen is accounted for under ASC 808, however, as ASC 808 does not address recognition or measurement matters such as determining the appropriate unit of accounting or when the recognition criteria are met, the Company accounts for the consideration received from Janssen in accordance with ASC 606. In accordance with ASC 606, the Company recognizes revenue when its customer or collaborator obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, it performs the following five steps:

- i. identify the contract(s) with a customer;
- ii. identify the performance obligations in the contract;
- iii. determine the transaction price;
- iv. allocate the transaction price to the performance obligations within the contract; and
- v. recognize revenue when (or as) the entity satisfies a performance obligation.

The Company only applies the five-step model to contracts when it determines that it is probable it will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer.

At contract inception, once the contract is determined to be by analogy within the scope of ASC 606, the Company assesses the goods or services promised within the contract to determine whether each promised good or service is a performance obligation. The promised goods or services in the Company's arrangements typically consist of a license to the Company's intellectual property and research, development and manufacturing services. The Company may provide options to additional items in such arrangements, which are accounted for as separate contracts when the customer elects to exercise such options, unless the option provides a material right to the customer. Performance obligations are promises in a contract to transfer a distinct good or service to the customer that (i) the customer can benefit from on its own or together with other readily available resources, and (ii) is separately identifiable from other promises in the contract. Goods or services that are not individually distinct performance obligations are combined with other promised goods or services until such combined group of promises meet the requirements of a performance obligation.

The Company determines transaction price based on the amount of consideration the Company expects to receive for transferring the promised goods or services in the contract. Consideration may be fixed, variable, or a combination of both. At contract inception for arrangements that include variable consideration, the Company estimates the probability and extent of consideration it expects to receive under the contract utilizing either the most likely amount method or expected amount method, whichever best estimates the amount expected to be received. The Company then considers any constraints on the variable consideration and includes in the transaction price variable consideration to the extent it is deemed probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

The Company then allocates the transaction price to each performance obligation based on the relative standalone selling price and recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) control is transferred to the customer and the performance obligation is satisfied. For performance obligations which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

The Company records amounts as accounts receivable when the right to consideration is deemed unconditional. When consideration is received, or such consideration is unconditionally due, from a customer prior to transferring goods or services to the customer under the terms of a contract, a contract liability is recorded as deferred revenue.

Amounts received prior to satisfying the revenue recognition criteria are recognized as deferred revenue in the Company's condensed consolidated balance sheet. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue – related party, current. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue – related party.

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The Company's collaboration revenue arrangements include the following:

**Up-front License Fees:** If a license is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from nonrefundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

**Milestone Payments:** At the inception of an agreement that includes research and development milestone payments, the Company evaluates each milestone to determine when and how much of the milestone to include in the transaction price. The Company first estimates the amount of the milestone payment that the Company could receive using either the expected value or the most likely amount approach. The Company primarily uses the most likely amount approach as that approach is generally most predictive for milestone payments with a binary outcome. Then, the Company considers whether any portion of that estimated amount is subject to the variable consideration constraint (that is, whether it is probable that a significant reversal of cumulative revenue would not occur upon resolution of the uncertainty.) The Company updates the estimate of variable consideration included in the transaction price at each reporting date which includes updating the assessment of the likely amount of consideration and the application of the constraint to reflect current facts and circumstances.

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

**Research and Development Services:** The Company is incurring research and development costs, with Janssen responsible for up to 100% of the costs, depending on the type of research and development services being performed. The Company will record costs associated with the development activities as research and development expenses in the condensed consolidated statement of operations and comprehensive loss consistent with ASC 730, *Research and Development*. The reimbursement of the research and development costs by Janssen is representative of the joint risk sharing nature of the arrangement. The Company considered the guidance in ASC 808 and will recognize the payments received from Janssen as a reduction to research and development expense when the related costs are incurred.

### ***Segment Information***

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

The Company's license revenue, research funding and deferred revenue from its License and Collaboration Agreement are generated in the United Kingdom.

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

	<b>September 30, 2019</b>	<b>December 31, 2018</b>
United States	\$ 13,390,438	\$ 454,568
United Kingdom	33,272,991	21,788,130
	<u>\$ 46,663,429</u>	<u>\$ 22,242,698</u>

### ***Accounting Pronouncements Recently Adopted***

In February 2016, the FASB issued ASUNo. 2016-02, *Leases* (“ASC 842” or “ASU 2016-02”). The amended guidance requires lessees to recognize lease liabilities and right-of-use assets on the balance sheet for all leases with initial terms longer than 12 months and provides enhanced disclosures on key information of leasing arrangements. In July 2018, further amendments were issued to clarify how to apply certain aspects of the amended lease guidance and to address certain implementation issues. The amended guidance was effective for the Company commencing on January 1, 2019. The adoption of the amended guidance materially affected our consolidated balance sheet and the primary impact was the recognition of minimum commitments at present value of our noncancelable operating leases as lease liabilities and corresponding right-of-use assets. In July 2018, the FASB issued ASU No. 2018-10, which provided narrow amendments to ASU 2016-02 to clarify how to apply the rate implicit in the lease, impairment of the net investment in the lease, lessee reassessment of lease classification, variable payments that depend on an index or rate and certain transition adjustments. In July 2018, the FASB also issued ASU No. 2018-11, which provides targeted improvements to ASU 2016-02 to provide entities the transition option to not apply the standard in the comparative periods presented in the year of adoption. The Company adopted the new standards effective January 1, 2019 using the modified retrospective transition method using the package of practical expedients and a discount rate of 8%, and elected to not apply the standard in the comparative periods presented in the year of adoption. Upon implementation, we recorded a right-of-use asset of \$10,836,319, which included a reclassification from property and equipment of a fully paid lease entered into in 2018 in the amount of \$7,321,251, and a corresponding lease obligation of \$3,716,336.

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. This update was effective for the Company as of January 1, 2019. The adoption of the provisions of ASU 2016-16 did not have a material impact on the current financial statements.

In July 2019, the FASB issued ASU 2019-07, *Codification Updates to SEC Sections—Amendments to SEC Paragraphs Pursuant to SEC Final Rule Releases No. 33-10532, Disclosure Update and Simplification, and Nos. 33-10231 and 33-10442, Investment Company Reporting Modernization and Miscellaneous Updates (SEC Update)*. ASU 2019-07 clarifies or improves the disclosure and presentation requirements of a variety of codification topics by aligning them with the SEC’s regulations, thereby eliminating redundancies and making the codification easier to apply. ASU 2019-07 became effective upon issuance and the adoption of ASU 2019-07, which is applied prospectively, did not have an impact on the Company’s current financial statements.

### ***Recent Accounting Pronouncements Not Yet Adopted***

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which adds a new Topic 326 to the Codification and removes the thresholds that companies apply to measure credit losses on financial instruments measured at amortized cost, such as loans, receivables, and held-to-maturity debt securities. Under current GAAP, companies generally recognize credit losses when it is probable that the loss has been incurred. The revised guidance will remove all recognition thresholds and will require companies to recognize an allowance for credit losses for the difference between the amortized cost basis of a financial instrument and the amount of amortized cost that the company expects to collect over the instrument’s contractual life. ASU 2016-13 also amends the credit loss measurement guidance for available-for-sale debt securities and beneficial interests in securitized financial assets. The guidance is applicable for fiscal years beginning after December 15, 2019 and interim periods within those years however, the FASB is expected to extend the effective date for smaller reporting companies to fiscal years beginning after December 15, 2022. The Company is currently evaluating the potential impact of the adoption of this standard on its related disclosures.

In August 2018, the FASB issued ASU 2018-13, *Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurements* which changes the fair value measurement disclosure requirements of ASC 820. The goal of the ASU is to improve the effectiveness of ASC 820’s disclosure requirements by providing users of the financial statements with better information about assets and liabilities measured at fair value in the financial statements and notes thereto. The guidance is applicable for fiscal years beginning after December 15, 2019 and interim periods within those years. The Company is currently evaluating the potential impact of the adoption of this standard on its related disclosures.

In November 2018, the FASB issued ASUNo. 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606* (“ASU 2018-18”). The standard amends Accounting Standards Codification 808, *Collaborative Arrangements* and Accounting Standards Codification 606, *Revenue from Contracts with Customers*, to clarify the interaction between collaborative arrangement participants that should be accounted for as revenue under ASC 606. In transactions when the collaborative arrangement participant is a customer in the context of a unit of account, revenue should be accounted for using the guidance in Topic 606. The amendments in ASU 2018-18 are effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. The Company is currently evaluating the new guidance included in ASU 2018-18, but does not expect it to have a material impact on its consolidated financial statements.

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**3. Accrued Expenses**

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

	<b>September 30, 2019</b>	<b>December 31, 2018</b>
Clinical Trial Costs	\$ 5,509,493	\$ 4,013,094
Compensation and Benefits	1,216,081	5,731,438
Consulting	1,049,451	821,009
Professional Fees	719,222	914,540
Manufacturing Costs	146,160	—
Rent	94,688	122,770
Interest	60,032	40,800
Research and Development	8,145	236,271
Other	543,623	111,775
	<u>\$ 9,346,895</u>	<u>\$ 11,991,697</u>

**4. Share-Based Compensation**

***2018 Incentive Award Plan and 2016 Equity Incentive Plan***

The Company's 2018 Incentive Award Plan and 2016 Equity Incentive Plan (collectively the "Plans"), were adopted by the Company's board of directors and shareholders. Under the Plans, the Company has granted share options to selected officers, employees and non-employee consultants. The Company's board of directors administers the Plans. Options granted under the Plans have a maximum contractual term of ten years. Options granted generally vest 25% on the first anniversary of the date of grant and the balance ratably over the next 36 months. Options granted to directors generally vest on the first anniversary of the 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, 2019 is as follows:

	Number of Options	Weighted-Average Exercise Price	Aggregate Intrinsic Value
Outstanding at December 31, 2018	3,254,365	\$ 7.64	\$ 6,903,313
Granted	500,000	18.44	
Exercised	(9,349)	(5.84)	
Forfeited	(21,319)	(9.39)	
Outstanding at September 30, 2019	<u>3,723,697</u>	<u>\$ 9.08</u>	<u>\$ 26,795,585</u>
Weighted average remaining contractual life of options outstanding as of December 31, 2018 (yrs)	<u>9.24</u>		
Weighted average remaining contractual life of options outstanding as of September 30, 2019 (yrs)	<u>8.60</u>		
Options exercisable at December 31, 2018	<u>535,241</u>	<u>\$ 5.79</u>	
Options exercisable at September 30, 2019	<u>1,098,211</u>	<u>\$ 6.11</u>	
Weighted average remaining contractual life of options exercisable as of December 31, 2018 (yrs)	<u>7.88</u>		
Weighted average remaining contractual life of options exercisable as of September 30, 2019 (yrs)	<u>7.52</u>		

The total fair value of options vested during the three-month periods ended September 30, 2019 and 2018 was \$429,647 and \$503,828, respectively.

The total fair value of options vested during the nine-month periods ended September 30, 2019 and 2018 was \$2,718,315 and \$1,060,177, respectively.

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During the three-month periods ended September 30, 2019 and 2018, the Company granted 195,000 and 0 share options, respectively.

During the nine-month periods ended September 30, 2019 and 2018, the Company granted 500,000 and 695,685 share options, respectively.

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>2019</u>	<u>2018</u>
Risk-free interest rate	2.03 - 2.55%	2.32% - 2.84%
Expected volatility	90%	90%
Expected dividend yield	0%	0%
Expected life (in years)	6.1	5.5 - 9.5

As of September 30, 2019, the total compensation expense relating to unvested options granted that had not yet been recognized was \$18,626,465, which is expected to be realized over a period of 3.75 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, 2019 and 2018 was \$13.86 and \$4.46, 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 the related share-based compensation expense was included in loss from operations over the requisite service period. As of September 30, 2019, 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 Securities and Exchange Commission ("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 \$5,587,546 and \$3,405,274, of which \$3,265,872 and \$1,992,182 was share-based, was recorded as general and administrative expense during the three-month periods ended September 30, 2019 and 2018, respectively.

Total compensation expense in connection with the issuance of those restricted ordinary shares, in the amount of \$11,840,200 and \$17,026,140, of which \$4,898,808 and \$8,523,932 was share-based, was recorded as general and administrative expense during the nine-month periods ended September 30, 2019 and 2018, respectively.

A summary of the restricted ordinary shares is as follows:

	<u>Ordinary Shares</u>	<u>\$ Value</u>
Non-vested at December 31, 2018	653,174	\$ 9,797,610
Vested during nine-month period ended September 30, 2019	(326,586)	(4,898,790)
Non-vested at September 30, 2019	<u>326,588</u>	<u>\$ 4,898,820</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.

During the three-month and nine-month periods ended September 30, 2019 and 2018 the Company recognized total share-based compensation expense in the accompanying condensed consolidated statements of operations and comprehensive loss as follows:

	<b>Three-month periods ended September 30,</b>	
	<b>2019</b>	<b>2018</b>
Research and development	\$ 1,131,659	\$ 1,040,499
General and administrative	2,373,892	1,881,858
<b>Total share based compensation</b>	<b>\$ 3,505,551</b>	<b>\$ 2,922,357</b>

  

	<b>Nine-month periods ended September 30,</b>	
	<b>2019</b>	<b>2018</b>
Research and development	\$ 2,828,944	\$ 2,931,010
General and administrative	7,997,721	12,624,903
<b>Total share based compensation</b>	<b>\$ 10,826,665</b>	<b>\$ 15,555,913</b>

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, 2019 and 2018.

## **5. Ordinary Shares**

### **Private Placement**

On February 27, 2019, the Company issued 5,797,102 ordinary shares in a private placement for gross proceeds of \$80 million, excluding offering costs of approximately \$2.4 million. Johnson & Johnson Innovation – JJDC, Inc. (“JJDC”), the investment arm of Johnson and Johnson and owner of Janssen, purchased 2,898,550 of the ordinary shares issued on the same terms and conditions as the other investors in the offering.

In connection with the offering, the Company also entered into a registration rights agreement whereby, promptly following the date on which the Company becomes eligible to use a registration statement on Form S-3, but in no event later than July 31, 2019, the Company shall prepare and file a registration statement covering the resale of all of the Registrable Securities, as defined in the agreement. The Company filed the Form S-3 on July 2, 2019 and the Form S-3 was declared effective on July 16, 2019.

### **Public Offering**

On August 7, 2019, the Company issued 3,200,000 ordinary shares in a public offering for gross proceeds of \$75 million, excluding offering costs of approximately \$5.1 million.

### **License Agreement**

As discussed in Note 8, on March 21, 2019, the Company issued 158,832 ordinary shares in connection with a license agreement. In accordance with the license agreement, the cost basis of the shares was based on the closing share price on January 31, 2019.

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## 6. Net Loss per Ordinary Share

The Company computes net loss per share in accordance with ASC260-10, *Earnings per Share* (see Note 2).

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

	Three-month periods ended September 30,	
	2019	2018
Net loss - basic and diluted	<u>\$(10,460,854)</u>	<u>\$(15,424,944)</u>
Weighted-average ordinary shares outstanding:		
Basic and Diluted	34,663,623	26,340,450
Net loss per share:		
Basic and Diluted	<u>\$ (0.30)</u>	<u>\$ (0.59)</u>

  

	Nine-month periods ended September 30,	
	2019	2018
Net loss - basic and diluted	<u>\$(49,265,184)</u>	<u>\$(61,809,129)</u>
Accretion of Preferred Shares financing costs	—	(761,012)
Accretion of warrant	—	(1,045,500)
Adjusted net loss - basic and diluted	<u>\$(49,265,184)</u>	<u>\$(63,615,641)</u>
Weighted-average ordinary shares outstanding:		
Basic and Diluted	32,111,733	16,355,849
Adjusted net loss per ordinary share:		
Basic and Diluted	<u>\$ (1.53)</u>	<u>\$ (3.89)</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, 2019	September 30, 2018
Restricted ordinary shares subject to forfeiture	326,588	762,036
Share options	3,723,697	1,629,687
	<u>4,050,285</u>	<u>2,391,723</u>

## 7. Income Taxes

The Company did not record a provision for income taxes for the three-month and nine-month periods ended September 30, 2019 and 2018, 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, 2019. 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.

The intraperiod tax allocation guidance requires that we allocate income taxes between continuing operations and other categories of earnings. When we have a year-to-date pre-tax loss from continuing operations and year-to-date pre-tax income in other comprehensive income, applicable GAAP (ASC 740-20-45-7) requires that we allocate the income tax provision to other categories of earnings (including other comprehensive income), and then record a related tax benefit in operations. For the three and nine-month periods ended September 30, 2019, we recognized net income from other comprehensive income while sustaining losses from operations. Because of the required allocation, we recorded an income tax benefit of \$338,670 and \$430,060, for the three and nine-month periods ended September 30, 2019, respectively, within "benefit for income taxes" and income tax expense of \$338,670 and \$430,060 within "other comprehensive income" on the Condensed Consolidated Statements of Operations and Comprehensive Loss for the three-month and nine-month periods ended September 30, 2019, respectively.

## 8. Related Party Transactions

### *Collaboration and License Agreements*

#### Janssen Pharmaceuticals, Inc.

On January 30, 2019, the Company entered into a Collaboration Agreement with Janssen for the research, development and commercialization of gene therapies for the treatment of inherited retinal diseases (“IRD”). Under the agreement, Janssen paid the Company a non-refundable upfront fee of \$100.0 million. Janssen and the Company will collaborate to develop the Company’s current clinical programs in retinitis pigmentosa and two genetic forms of achromatopsia and Janssen has the exclusive right to commercialize these three product candidates (“Clinical IRD Product Candidates”) globally.

Pursuant to the Collaboration Agreement, the Company and Janssen also agreed on a research collaboration to develop a pipeline of preclinical inherited retinal disease gene therapy candidates (“Research IRD Product Candidates”). The parties will select and prioritize the Research IRD Product Candidates and Janssen has the right to opt-in for a fee for each of the specified targets (each an “Option Target”) to obtain certain development, manufacturing and commercialization rights for the Research IRD Product Candidates.

Unless terminated earlier under certain termination clauses, the Collaboration Agreement will continue in effect, on a product-by-product and country-by-country basis, until such time as the royalty terms expires in such country. The Company has determined enforceable rights exist in the Collaboration Agreement as the termination clauses are substantive termination penalties by way of the non-refundable upfront fee and the reversion of any licensed intellectual property granted to Janssen upon the termination of the agreement.

On February 27, 2019, in connection with a private placement, the Company issued 2,898,550 ordinary shares to JJDC, the investment arm of Johnson and Johnson and owner of Janssen, on the same terms and conditions as the other investors in the offering. After the offering, JJDC became a related party.

#### *Clinical IRD Product Candidates*

Under the Collaboration Agreement, the Company and Janssen will jointly develop Clinical IRD Product Candidates to permit Janssen to commercialize such Clinical IRD Product Candidates under an exclusive license from the Company. In general, the Company will have the primary responsibility to develop each Clinical IRD Product Candidate in accordance with the development plan for each Clinical IRD Product Candidate, including where applicable, conducting any necessary research in order to submit the applicable regulatory filings to regulatory authorities. The Company will manufacture these products in its cGMP manufacturing facility for both clinical and commercial supply. Janssen will pay 100% of the clinical and commercialization costs of the products and the Company is eligible to receive untiered 20% royalties on net sales of products and additional development and commercialization milestones up to \$340.0 million.

#### *Research IRD Product Candidates*

Under the Collaboration Agreement, the Company and Janssen will collaborate to develop Research IRD Product Candidates, with Janssen paying for the majority of the research costs. Janssen has the right to exclusively license any product coming out of the collaboration at the time of an investigational new drug application (“IND”) for an additional fee for each Research IRD Product Candidate. Janssen will then pay 100% of the clinical and commercialization costs for these Research IRD Product Candidates and the Company will receive an untiered royalty on net sales in the high teens as well as development milestones for each Research IRD Product Candidate.

#### *Revenue Recognition under the Collaboration Agreement*

The Collaboration Agreement is accounted for under ASC 808, however, ASC 808 does not address recognition or measurement matters. Therefore, the Company will account for the recognition and measurement of consideration under ASC 606. In determining the appropriate amount of revenue to be recognized under ASC 606, the Company performed the following steps: (i) identified the promised goods or services in the contract; (ii) determined whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company evaluated the potential performance obligations in the contract, which included the exclusive license to Clinical IRD Product Candidates, the research, development and manufacturing services (“the services”), and the participation in various joint committees and determined that none of the performance obligations by themselves were distinct. Goods and services that are not distinct are bundled with other goods or services in the contract until a bundle of goods or services that is distinct is created. The services, when combined with the licenses, represent a bundle and should be accounted for as a single performance obligation due to the

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relevance of the services to the value of the early-stage license and the potential for the intellectual property to be significantly modified during the services period. The Company also evaluated whether or not the right to purchase exclusive option rights for specified Research IRD Product Candidates represents future performance obligations and concluded that these represent a separate buyer decision at market rates, rather than a material right performance obligation. As such, these options have been excluded from the initial allocation of transaction price and the Company will account for these options as separate contracts when and if the Janssen elects to exercise the options.

Under ASC 606, the Company recognized collaboration revenue using the cost-to-cost input method, which it believes best depicts the transfer of control to the customer. Under the cost-to-cost input method, the extent of progress towards completion is measured based on the ratio of actual costs incurred to the total estimated costs expected upon satisfying the combined performance obligation by the potential product candidate. Under this method, revenue will be recorded as a percentage of the estimated transaction price based on the extent of progress towards completion. Under ASC 606, the estimated transaction price will include variable consideration. The Company does not include variable consideration to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will occur when any uncertainty associated with the variable consideration is resolved. The estimate of the Company's measure of progress and estimate of variable consideration to be included in the transaction price will be updated at each reporting date as a change in estimate. The amount related to the unsatisfied portion will be recognized as that portion is satisfied over time.

Under ASC 606 the Company accounts for (i) the licenses it conveyed with respect to the Clinical IRD Product Candidates and (ii) its obligations to perform services as a single performance obligation under the Collaboration Agreement with Janssen on a product candidate basis. Janssen's right to purchase exclusive options to obtain certain development, manufacturing and commercialization rights are accounted for separately as they do not represent material rights, based on the criteria of ASC 606. Upon the exercise of any purchased option by Janssen, the contract promises associated with an Option Target would use a separate cost-to-cost model for purposes of revenue recognition under ASC 606.

During the nine months ended September 30, 2019, the Company received a \$100.0 million non-refundable upfront fee from Janssen and allocated this amount plus other variable consideration not subject to constraint to each identified performance obligation using a combination of methods allowable under ASC 606. The Company applies the practical expedient in Topic 606 and does not include disclosures regarding amounts for variable consideration allocated to wholly-unsatisfied performance obligations or wholly-unsatisfied distinct goods that form part of a single performance obligation, if any. This variable consideration includes expected reimbursement of research and development costs. During the three-month and nine-month periods ended September 30, 2019, the Company recognized \$3,582,586 and \$6,349,222, respectively, of the deferred revenue – related party as license revenue. The Company also recognized \$9,303,405 and \$13,319,084, respectively, during the three-month and nine-month periods ended September 30, 2019 related to the reimbursement of research and development expenses which was recorded as an offset to research and development expenses. As of September 30, 2019, the Company expects to recognize the remaining \$93,650,778 in deferred revenue associated with the non-refundable upfront fee over the estimated research and development period using the cost-to-cost input method over an estimated period of approximately 7.25 years.

### Riboswitch Research Collaboration Agreement

On October 16, 2018, the Company entered into a Riboswitch research collaboration agreement with Janssen, 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.

Upon execution of the agreement, Janssen paid the stage 1 fee in the amount of \$658,667 and such payment was recorded as deferred revenue – related party. The stage 1 fee was being amortized over the estimated research term of eight months. During the three-month and nine-month periods ended September 30, 2019, the Company amortized \$0 and \$444,399, respectively, of the deferred revenue, which was recorded as an offset to research and development expenses. Additionally, the stage two fee, in the amount of \$328,524 was recorded and fully amortized during the three-month period ended September 30, 2019. As of September 30, 2019, the stage 1 and stage 2 fees have been fully amortized.

### 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. 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, 2019 and 2018 were approximately \$72,000 and \$137,000, respectively.

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Total research and development expenses under this agreement for the nine-month periods ended September 30, 2019 and 2018 were approximately \$245,000 and \$509,000, respectively.

Future obligations, under the agreement equal £82,941, or approximately \$101,931, through October 2020.

The amount due to UCL under this master services agreement at September 30, 2019 and December 31, 2018 is \$480,825 and \$389,101, respectively, and is included in accounts payable and accrued expenses on the condensed consolidated balance sheets.

### ***License Agreement***

Effective February 4, 2015, 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 had agreed to pay UCL Business certain sales milestone payments, if achieved, in the aggregate amount of £39.8 million, or approximately \$48.9 million using the exchange rate at September 30, 2019, 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 \$65,000, until the first commercial sale of a product. The agreement terminates 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.

On January 29, 2019, the Company amended and restated the following agreements: (i) the License Agreement, dated February 4, 2015, as amended, between the Company and UCL Business; (ii) the License Agreement, dated July 28, 2017, as amended, between the Company and UCL Business; and (iii) the License Agreement, dated March 15, 2018, between the Company and UCL Business to establish new stand-alone license agreements for the following inherited retinal disease programs: (a) achromatopsia (“ACHM”) caused by mutations in CNGB3; (b) ACHM caused by mutations in CNGA3; (c) X-linked retinitis pigmentosa (“XLRP”); and (d) RPE65-mediated IRD.

The Company’s obligation to pay UCL Business a share of certain sublicensing revenues, as was provided under the February 4, 2015 agreement, has been removed from each of the stand-alone agreements with respect to the IRD programs listed above. Each of the stand-alone agreements now reflects terms substantially similar to those of the February 4, 2015 agreement.

Additionally, under the new stand-alone agreement related to CNGB3 the Company paid UCL Business an upfront payment of £1,500,000, or approximately \$1,976,000, and issued 158,832 of the Company’s ordinary shares, which were valued at £1,500,000, or approximately \$1,966,000.

The Company did not incur any research and development expenses under the agreements during the three-month periods ended September 30, 2019 and 2018.

The Company incurred research and development expenses under the agreements in the amount of \$4,111,876, inclusive of the amendment payments of approximately \$3,942,000, and \$219,863 during the nine-month periods ended September 30, 2019 and 2018, respectively.

### ***Leases***

#### ***ARE Lease***

Effective July 1, 2016, the Company entered into a non-cancellable operating lease (the “ARE Lease”) for laboratory and related office facilities in New York with ARE-East River Science Park, LLC (“ARE”). The ARE 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 December 31, 2018, the balance of deferred rent, representing the difference between cash rent paid and straight-line rent expense, was \$201,264. As of September 30, 2019, and in accordance with ASC 842, the difference between cash rent paid and straight-line rent expense of \$167,480 is reflected in the right-of-use asset.

Total rent expense under this operating lease was \$121,890 and \$121,888 for the three-month periods ended September 30, 2019 and 2018, respectively.

Total rent expense under this operating lease was \$365,666 and \$365,668 for the nine-month periods ended September 30, 2019 and 2018, respectively.

As of September 30, 2019, the aggregate future minimum rental payments under this lease are \$1,264,493.

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 initially expired 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.

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The aggregate future minimum rental payments under this lease as of September 30, 2019 for years ending December 31 are as follows:

2019	\$ 136,224
2020	554,432
2021	<u>573,837</u>
Total future rent payments	<u>\$1,264,493</u>

### Kadmon Lease

The Company is currently leasing office space on a month-to-month basis from Kadmon Corporation, LLC (“Kadmon”).

During the three-month periods ended September 30, 2019 and 2018, the Company incurred rent charges from Kadmon, in the amount of \$145,755 and \$140,805, respectively, which are included in loss from operations.

During the nine-month periods ended September 30, 2019 and 2018, the Company incurred rent charges from Kadmon, in the amount of \$430,649 and \$416,479, respectively, which are included in loss from operations.

During the three-month periods ended September 30, 2019 and 2018, the Company made cash payments totaling \$145,755 and \$140,954, respectively, to Kadmon.

During the nine-month periods ended September 30, 2019 and 2018, the Company made cash payments totaling \$430,649 and \$1,284,258, respectively, to Kadmon.

The were no amounts due to Kadmon at September 30, 2019 and December 31, 2018.

## 9. Leases

We account for leases in accordance with ASC 842. We determine if an arrangement is a lease at contract inception. A lease exists when a contract conveys the right to control the use of identified property, plant, or equipment for a period of time in exchange for consideration. The definition of a lease embodies two conditions: (1) there is an identified asset in the contract that is land or a depreciable asset (i.e., property, plant, and equipment), and (2) we have the right to control the use of the identified asset. We account for the lease and non-lease components as a single lease component.

From time to time we enter into direct financing lease arrangements that include a lessee obligation to purchase the leased asset at the end of the lease term, a bargain purchase option, or provides for minimum lease payments with a present value of 90% or more of the fair value of the leased asset at the date of lease inception.

Operating leases where we are the lessee are included in right-of-use (“ROU”) assets and lease obligations are included on our condensed consolidated balance sheets. The lease obligations are initially and subsequently measured at the present value of the unpaid lease payments at the lease commencement date and subsequent reporting periods.

Finance leases where we are the lessee are included in ROU assets and lease obligations on our condensed consolidated balance sheets. The lease obligations are initially measured in the same manner as for operating leases and are subsequently measured at amortized cost using the effective interest method.

Key estimates and judgments include how we determined (1) the discount rate we use to discount the unpaid lease payments to present value, (2) lease term and (3) lease payments.

ASC 842 requires a lessee to discount its unpaid lease payments using the interest rate implicit in the lease or, if that rate cannot be readily determined, its incremental borrowing rate. As most of our leases where we are the lessee do not provide an implicit rate, we use our incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments. Our incremental borrowing rate for a lease is the rate of interest we would have to pay on a collateralized basis to borrow an amount equal to the lease payments under similar terms. We use the implicit rate when readily determinable.

The lease term for all of our leases includes thenon-cancellable period of the lease plus any additional periods covered by either a lessee option to extend (or not to terminate) the lease that is reasonably certain to be exercised, or an option to extend (or not to terminate) the lease controlled by the lessor.

The ROU asset is initially measured at cost, which comprises the initial amount of the lease liability adjusted for lease payments made at or before the lease commencement date less any lease incentives received.

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For operating leases, the ROU asset is subsequently measured throughout the lease term at the carrying amount of the lease liability, minus any accrued lease payments, less the unamortized balance of lease incentives received. Lease expense for lease payments is recognized on a straight-line basis over the lease term.

For finance leases, the ROU asset is subsequently amortized using the straight-line method from the lease commencement date to the earlier of the end of its useful life or the end of the lease term unless the lease transfers ownership of the underlying asset to us, or we are reasonably certain to exercise an option to purchase the underlying asset. In those cases, the ROU asset is amortized over the useful life of the underlying asset. Amortization of the ROU asset is recognized and presented separately from interest expense on the lease liability.

We have elected not to recognize ROU assets and lease liabilities for all short-term leases that have a lease term of 12 months or less at lease commencement. We recognize the lease payments associated with our short-term leases as an expense on a straight-line basis over the lease term.

We adopted ASU 2016-02 using a modified retrospective transition approach as of the effective date as permitted by the amendments in ASU2018-11, which provides an alternative modified retrospective transition method. As a result, we were not required to adjust our comparative period financial information for effects of the standard or make the new required lease disclosures for periods before the date of adoption (i.e., January 1, 2019). We have elected to adopt the package of transition practical expedients and, therefore, have not reassessed (1) whether existing or expired contracts contain a lease, (2) lease classification for existing or expired leases or (3) the accounting for initial direct costs that were previously capitalized. We did not elect the practical expedient to use hindsight for leases existing at the adoption date. Further, we do not expect the amendments in ASU 2018-01: *Land Easement Practical Expedient* to have an effect on us because we do not enter into land easement arrangements.

### New York Sublease

Effective May 31, 2019, the Company entered into a non-cancelable operating sublease with a non-related third party for laboratory and office space in New York. The lease, which expires on October 31, 2026, provides for monthly base rent and property management fees, including rent escalations and rent holidays, plus operating expenses during the lease term. The Company records monthly rent expense on a straight-line basis from June 20, 2019, the date the Company was allowed to access the leased premises, through October 31, 2026, when the sublease is set to terminate. In conjunction with this operating sublease, the Company recognized an initial operating lease right-of-use asset and corresponding operating lease liability of \$12.2 million which is included in right-of-use assets and lease obligations on the condensed consolidated balance sheets.

There were cash payments made under this operating lease for the three-month and nine-month periods ended September 30, 2019.

Total rent expense recognized under this operating lease was \$90,000 for the three-month and nine-month periods ended September 30, 2019.

### Tudor Street Lease

Effective June 11, 2019, the Company entered into a non-cancelable operating lease with a non-related third party for warehouse space in London. The lease, which expires on June 10, 2029, provides for quarterly base rent and operating expenses during the lease term. The Company has the right to terminate this lease on June 10, 2024 by giving the landlord notice at least six months prior to such date. If the Company does not terminate the lease on June 10, 2024, the annual rent is subject to a one-time adjustment based on the then current market conditions on June 11, 2024. As the Company does not expect to exercise its right to terminate the lease prior to the expiration date, the Company records monthly rent expense on a straight-line basis from June 11, 2019, the date the Company took possession of the leased premises, through June 10, 2029, when the lease is set to terminate. In conjunction with this operating lease, the Company recognized an initial operating lease right-of-use asset and corresponding operating lease liability of £1.2 million, or approximately \$1.5 million, which is included in right-of-use assets and lease obligations on the condensed consolidated balance sheets.

Total cash payments made under this operating lease were £42,600, or approximately \$52,000, for the three-month period ended September 30, 2019.

Total rent expense recognized under this operating lease was £85,200, or approximately \$105,000, for the three-month period ended September 30, 2019.

### Provost Street Lease

On May 29, 2019, Meira UK II entered into an Agreement for Lease with an unrelated third party which provided a license to lease an entire building consisting of five floors of office and laboratory space in London. The leased premises were being renovated by the landlord with such renovations being completed in September 2019. Upon completion of the landlord renovations, the Company entered into a non-cancellable operating lease, which expires on September 8, 2029. The lease provides for quarterly base rent, including a rent holiday at the commencement of the lease, plus operating expenses during the lease term. The Company has the right to terminate this lease on September 8, 2024 by giving the landlord notice at least six months prior to such date. If the Company does not terminate the lease on September 8, 2024, the annual rent is subject to a one-time adjustment based on the then current market conditions on September 9, 2024. As the Company does not expect to exercise its right to terminate the lease prior to the expiration date, the Company records monthly rent expense on a straight-line basis from September 11, 2019, the date the Company took possession of the lease, through September 8, 2029 when the lease is set to terminate. In conjunction with this operating lease, the Company recognized an operating lease right-of-use asset and corresponding operating lease liability of £4.8 million, or approximately \$5.9 million using the exchange rate at September 30, 2019, which is included in right-of-use assets and lease obligations on the condensed consolidated balance sheets.

Total cash payments made under this operating lease were £0, for the three-month period ended September 30, 2019.

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Total rent expense recognized under this operating lease was £0 for the three-month period ended September 30, 2019.

We have commitments under operating leases for laboratory and office space. We also have finance leases for manufacturing space and office equipment. Our leases have initial lease terms ranging from 3 years to 108 years. Certain lease agreements contain provisions for future rent increases. Payments due under the lease contracts include fixed payments.

As of September 30, 2019, we have short term lease commitments amounting to approximately \$100,000 on a monthly basis for three leases for office space that are month-to-month leases.

The components of lease cost for the three-month and nine-month periods ended September 30, 2019 are as follows:

	Three Months Ended 9/30/2019	Nine Months Ended 9/30/2019
<b>Finance lease cost</b>		
Amortization of right-of-use assets	\$ 64,181	\$ 218,552
Interest on lease liabilities	606	1,598
<b>Total Finance Lease Cost</b>	64,787	220,150
Operating lease cost	897,310	1,324,474
Short-term lease cost	245,385	904,166
<b>Total lease cost</b>	<u>\$ 1,207,482</u>	<u>\$2,448,790</u>

Amounts reported in the condensed consolidated balance sheets for leases where we are the lessee as of the period ended September 30, 2019 were as follows:

	September 30, 2019
<b>Operating leases</b>	
Right of Use Asset	22,106,415
Capitalized Lease Obligations	22,612,395
<b>Finance leases</b>	
Right-of-Use Asset	6,695,342
Capitalized Lease Obligations	16,371
<b>Weighted-Average Remaining Lease Term</b>	
Operating leases	8.1 years
Finance leases	107.3 years
<b>Weighted-Average Discount Rate</b>	
Operating Leases	8.5%
Finance Leases	6.9%

Other information related to leases as of the three-month and nine-month periods ended September 30, 2019 are as follows:

	Three Months Ended 9/30/2019	Nine Months Ended 9/30/2019
<b>Cash paid for amounts included in the measurement of lease liabilities</b>		
Operating cash flows from finance leases	6,857	20,223
Operating cash flows from operating leases	355,792	847,608
Financing cash flows from finance leases	321	1,313
<b>Right-of-use assets obtained in exchange for lease liabilities</b>		
Operating leases	5,938,426	22,932,582
Finance leases	—	—

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Future minimum lease payments under non-cancellable leases as of September 30, 2019 are as follows:

	Operating Leases	Finance Leases
2019	853,350	9,572
2020	4,012,039	7,179
2021	4,346,557	—
2022	3,839,442	—
2023	3,908,165	—
Thereafter	13,997,959	—
<b>Total undiscounted lease payments</b>	<b>30,957,512</b>	<b>16,751</b>
Less: Imputed interest	(8,345,117)	(380)
<b>Total lease liabilities</b>	<b>22,612,395</b>	<b>16,371</b>

**10. Commitments**

There were no new material commitments entered into during the nine months ended September 30, 2019.

**11. Subsequent Events**

Management has evaluated subsequent events through the date of this filing. Based on its evaluation, there were no subsequent events to report.

## 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 ("Form 10-Q") and those included in our Annual Report on Form 10-K for the year ended December 31, 2018 (the "Form 10-K"). Some of the information contained in this discussion and analysis or set forth elsewhere in the Form 10-Q, 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 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 MeiraGTx Holdings plc and its subsidiaries.*

### Overview

We are a vertically integrated, clinical stage gene therapy company with six programs in clinical development 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. Led by an experienced management team, 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 ophthalmology, salivary gland and neurodegenerative disease programs, 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 ("GAAP"). Since our formation, we have devoted substantially all of our resources to developing our technology platform, establishing our viral vector manufacturing facilities 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, developing our business plan, 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 amyotrophic lateral sclerosis ("ALS"). In October 2018, we acquired Vector Neurosciences, Inc., a Delaware corporation. In connection with that acquisition, we acquired its rights to the clinical stage gene therapy product candidate adeno-associated virus encoding glutamic acid decarboxylase ("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 Series A ordinary shares, Convertible Preferred C Shares and ordinary shares. Through September 30, 2019, we received gross proceeds of approximately \$358.7 million from sales of our ordinary shares, Series A ordinary shares and Convertible Preferred C Shares and \$100.0 million from the collaboration, option and license agreement with Janssen Pharmaceuticals, Inc. ("Janssen"), one of the Janssen Pharmaceuticals Companies of Johnson & Johnson (the "Collaboration and License Agreement"). As of September 30, 2019, we had cash and cash equivalents of \$253.3 million.

We are a clinical stage company and have not generated any product revenues to date. We have six 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, 2019 and 2018 were \$10.5 million and \$15.4 million, respectively. For the nine months ended September 30, 2019 and 2018, our net losses were \$49.3 million and \$61.8 million, respectively. As of September 30, 2019, we had an accumulated deficit of \$197.6 million. We do not expect to generate revenue from sales of any products for several years, if at all. In March 2019, we received an upfront payment in the amount of \$100.0 million from the Collaboration and License Agreement. Additionally, pursuant to the Collaboration and License Agreement, we are eligible to receive research and development funding and potential milestone payments and royalties.

Our total operating expenses were \$59.2 million and \$58.0 million for the nine months ended September 30, 2019 and 2018, respectively. While we expect our operating expenses to increase substantially in connection with our ongoing development activities related to our product candidates, we believe that these increases will be partially offset by the research funding in connection with the Collaboration and License Agreement. We anticipate that our expenses will increase due to costs associated with our clinical development program targeting achromatopsia due to mutations in the *CNGB3* or *CNGA3* gene, inherited retinal dystrophy caused by mutations in *RPE65*, and X-linked retinitis pigmentosa, or XLRP. In addition, we expect to continue incurring increasing costs associated with our clinical activities for *AAV-AQP1* for the treatment of radiation-induced xerostomia and xerostomia associated with Sjogren's syndrome. We are currently working with regulatory agencies to determine the path forward for clinical development of AAV-GAD. 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 operations, 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.

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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 continue incurring 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 cash and cash equivalents at September 30, 2019, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into 2022. 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 and scaling our manufacturing facilities and processes;
- the costs of operating as a public company;
- the extent to which we in-license or acquire rights to other products, product candidates 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.

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.

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### Highlights and Recent Development

#### Clinical Development Highlights

**AAV-RPE65 for RPE65-Deficiency Associated Retinal Dystrophy:** In May 2019, we reported positive 6-month data from the Phase 1/2 dose escalation trial of AAV-RPE65. The trial achieved the primary endpoint of safety and tolerability of AAV-RPE65. Additionally, AAV-RPE65 demonstrated statistically significant improvement across several secondary endpoints designed to assess clinical activity. Data from the trial were presented in September 2019 at the 52nd Annual Scientific Meeting of the Retina Society and in October 2019 at the American Academy of Ophthalmology Annual Meeting.

**AAV-GAD for Parkinson's Disease:** We are currently working with regulatory agencies to determine the path forward for clinical development of AAV-GAD.

**AAV-AQP1 for Grade 2/3 Radiation-Induced Xerostomia:** We initiated the multi-site, dose-finding, Phase 1/2 AQUAX trial of AAV-AQP1 in the third quarter of 2019. We are enrolling patients with radiation-induced Grade 2/3 xerostomia following treatment for head and neck cancer. A single center, Phase 1 dose-finding study of AAV-AQP1 also continues to enroll patients at the National Institutes of Health (NIH). Dosing was completed in the third dose escalation cohort at the NIH in the third quarter of 2019.

**Janssen-partnered investigational gene therapies:** We continue to advance a portfolio of gene therapies for the treatment of inherited retinal diseases with our partner, Janssen, including our ongoing Phase 1/2 studies of AAV-RPGR for X-linked retinitis pigmentosa (XLRP) and AAV-CNGB3 and AAV-CNGA3 for achromatopsia ("ACHM").

#### Corporate Highlights

**Expanding manufacturing capabilities:** In August 2019, we raised approximately \$75 million of gross proceeds in a public offering of approximately 3.2 million of our ordinary shares. We intend to use a portion of the proceeds of this offering to expand our manufacturing capabilities, including building a second cGMP viral vector manufacturing facility as well as a cGMP plasmid production facility. We are completing feasibility studies for our second facility and expect to begin construction in 2020.

### Components of Our Results of Operations

#### *License Revenue*

Our license revenue consisted of the amortization of the upfront payment we received in connection with the Collaboration and License Agreement.

#### *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.

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*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.

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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.

	Three Months Ended			Nine Months Ended		
	2019	September 30, 2018	Change	2019	September 30, 2018	Change
Ophthalmology program	\$ 2,900,513	\$ 1,153,238	\$ 1,747,275	\$ 7,593,387	\$ 3,922,392	\$ 3,670,995
Salivary gland program	768,053	208,763	559,290	2,435,034	643,998	1,791,036
Neurodegenerative diseases programs	875,932	661,872	214,060	2,761,198	1,723,578	1,037,620
Manufacturing	3,628,964	1,395,661	2,233,303	6,372,018	3,710,966	2,661,052
Other research and development costs	6,072,913	4,689,626	1,383,287	22,292,802	12,826,242	9,466,560
Research Funding	(9,631,929)	—	(9,631,929)	(14,092,007)	—	(14,092,007)
Total research and development expenses	<u>\$ 4,614,446</u>	<u>\$ 8,109,160</u>	<u>\$(3,494,714)</u>	<u>\$ 27,362,432</u>	<u>\$ 22,827,176</u>	<u>\$ 4,535,256</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.

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 gain (loss)*

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 Limited and MeiraGTx B.V. are measured using the foreign subsidiaries' local currency as the functional currency. MeiraGTx UK II Limited's 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.

**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. 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.

The Company's critical accounting policies, significant judgements and estimates are included in the Company's Form 10-K for the year ended December 31, 2018 and Note 2 to our unaudited condensed consolidated financial statements included elsewhere in this Form 10-Q.

***Recent Accounting Pronouncements***

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

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[Table of Contents](#)**Results of Operations****Comparison of Three Months Ended September 30, 2019 and 2018**

	2019	2018	Change
License revenue - related party	\$ 3,582,586	\$ —	\$ 3,582,586
Operating expenses:			
General and administrative	\$ 9,874,810	\$ 6,629,052	\$ 3,245,758
Research and development	4,614,446	8,109,160	(3,494,714)
Total operating expenses	14,489,256	14,738,212	(248,956)
Loss from operations	(10,906,670)	(14,738,212)	3,831,542
Other non-operating income (expense)			
Foreign currency gain (loss)	115,470	(677,488)	792,958
Interest income	959	264	695
Interest expense	(9,283)	(9,508)	225
Loss before income taxes	(10,799,524)	(15,424,944)	4,625,420
Benefit for income taxes	338,670	—	338,670
Net loss	<u>\$ (10,460,854)</u>	<u>\$ (15,424,944)</u>	<u>\$ 4,964,090</u>

*License Revenue*

License revenue in the amount of \$3.6 million for the three months ended September 30, 2019 represents amortization of the \$100.0 million upfront payment received in connection with the Collaboration and License Agreement

*General and Administrative Expenses*

General and administrative expenses were \$9.9 million for the three months ended September 30, 2019, compared to \$6.6 million for the three months ended September 30, 2018. The increase of \$3.3 million was primarily due to increases of \$1.6 million in payroll, \$0.5 million in insurance, \$0.4 million in rent, \$0.3 million in consulting fees and \$0.5 million in share-based compensation.

*Research and Development Expenses*

Research and development expenses for the three months ended September 30, 2019 were \$4.6 million, compared to \$8.1 million for the three months ended September 30, 2018. The decrease of \$3.5 million was primarily due to an increase of \$9.6 million in research funding provided by our license and collaboration agreements with Janssen, which was partially offset by an increase of \$3.2 million in costs related to our clinical trials and \$2.9 million in costs related to the manufacture of material for our clinical trials.

*Foreign Currency Gain (Loss)*

Foreign currency gain was \$0.1 million for the three months ended September 30, 2019 compared to a loss of \$0.7 million for the three months ended September 30, 2018. The increase of \$0.8 million was primarily due to a strengthening of the U.S. dollar against the pound sterling during the three months ended September 30, 2019.

[Table of Contents](#)**Results of Operations***Comparison of Nine Months Ended September 30, 2019 and 2018*

	2019	2018	Change
License revenue - related party	\$ 6,349,222	\$ —	\$ 6,349,222
Operating expenses:			
General and administrative	31,811,456	35,129,120	(3,317,664)
Research and development	27,362,432	22,827,176	4,535,256
Total operating expenses	59,173,888	57,956,296	1,217,592
Loss from operations	(52,824,666)	(57,956,296)	5,131,630
Other non-operating income (expense)			
Foreign currency gain (loss)	3,117,047	(2,425,488)	5,542,535
Change in fair value of warrant liability	—	(1,514,775)	1,514,775
Other income	—	83,075	(83,075)
Interest income	40,686	50,926	(10,240)
Interest expense	(28,311)	(46,571)	18,260
Loss before income taxes	(49,695,244)	(61,809,129)	12,113,885
Benefit for income taxes	430,060	—	430,060
Net loss	\$(49,265,184)	\$(61,809,129)	\$12,543,945

*License Revenue*

License revenue in the amount of \$6.3 million for the nine months ended September 30, 2019 represents amortization of the \$100.0 million upfront payment received in connection with the Collaboration and License Agreement.

*General and Administrative Expenses*

General and administrative expenses were \$31.8 million for the nine months ended September 30, 2019, compared to \$35.1 million for the nine months ended September 30, 2018. The decrease of \$3.3 million was primarily due to decreases of \$3.1 million in payroll and \$4.6 million in share-based compensation, which was partially offset by increases of \$1.9 million in legal and accounting fees, \$1.0 million in insurance expenses, \$0.5 million in rent expenses, \$0.5 million in travel expenses, \$0.2 million in consulting fees, \$0.2 million in director fees and \$0.1 million in other general and administrative expenses.

*Research and Development Expenses*

Research and development expenses for the nine months ended September 30, 2019 were \$27.4 million, compared to \$22.8 million for the nine months ended September 30, 2018. The increase of \$4.6 million was primarily due to an increase in costs of \$4.0 million related to the amendment of our license agreement with UCL, \$3.6 million in costs related to the manufacture of material for our clinical trials, \$7.2 million in costs related to our clinical trials, \$2.8 million in consulting fees, and \$1.1 million in other research and development expenses, which was partially offset by an increase of \$14.1 million in research funding provided by our license and collaboration agreements with Janssen.

*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, all of the outstanding warrants were exercised at which time the warrant liability was determined to be \$4.2 million, which represented the difference in the market value of the convertible 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 that time, which resulted in a loss being recorded for the nine months ended September 30, 2018. There were no warrants outstanding during the nine months ended September 30, 2019.

*Foreign Currency Gain (Loss)*

Foreign currency gain was \$3.1 million for the nine months ended September 30, 2019 compared to a loss of \$2.4 million for the nine months ended September 30, 2018. The increase of \$5.5 million was primarily due to a strengthening of the U.S. dollar against the pound sterling during the nine months ended September 30, 2019.

***Liquidity and Capital Resources***

Since our inception, we have incurred significant operating losses. For the nine months ended September 30, 2019, we generated \$42.0 million of positive cash flows from operations. However, prior to the nine months ended September 30, 2019, the Company did not generate positive cash flows from operations and there are no assurances that the Company will generate positive cash flows in the future. Additionally, 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 products manufactured to support preclinical studies and clinical trials, expanding our intellectual property portfolio, and providing general and administrative support for our operations. In addition, we expect to expand our manufacturing and supply chain capabilities in the coming months. 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.

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 executive chairman and founder 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, 2019, the restricted cash balances for the ARE lease were invested in a commercial money market account. We had \$123,376 of restricted cash included in long-term assets as of September 30, 2019. This restricted cash balance is for the ARE lease and is expected to remain at \$123,376 through the end of the lease term in December 2021, plus three months. We do not currently have any approved products and have never generated any revenue from product sales. We have historically financed our operations primarily through cash on hand and proceeds from the sale of our ordinary shares, Series A ordinary shares and convertible preferred C shares. In March 2019, we received \$100.0 million in connection with the Collaboration and License Agreement, which provides us with research funding, and we are eligible to receive potential milestone payments and royalties.

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[Table of Contents](#)**Cash Flows**

As of September 30, 2019, we had \$253.3 million of cash and cash equivalents.

	For the nine-month periods ended September 30,	
	2019	2018
Net cash provided by (used in) operating activities	\$ 42,016,287	\$ (47,419,158)
Net cash used in investing activities	(4,230,740)	(2,372,622)
Net cash provided by financing activities	147,766,947	130,047,495
Increase in cash	<u>\$ 185,552,494</u>	<u>\$ 80,255,715</u>

*Operating Activities*

During the nine months ended September 30, 2019, our cash provided by operating activities of \$42.0 million was primarily due to our receipt of a \$100.0 million upfront payment received from the Collaboration and License Agreement, which was partially offset by a net loss of \$49.3 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 net loss included non-cash charges of \$17.5 million, which consisted of \$10.8 million of share-based compensation, \$2.0 million for shares issued in connection with license agreements, depreciation of \$1.6 million, which was partially offset by a foreign currency gain of \$3.1 million. Additionally, operating assets, consisting of prepaid expenses, security deposits and other current assets, increased by \$11.5 million and operating liabilities, consisting of accounts payable, accrued expenses and other liabilities, decreased by \$1.5 million and deferred revenue increased by \$93.1 million.

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.

*Investing Activities*

Net cash used in investing activities for the nine months ended September 30, 2019 and 2018 of \$4.2 million and \$2.4 million, respectively, consisted of purchases of property and equipment, primarily for our manufacturing and process development facilities.

*Financing Activities*

Net cash provided by financing activities was \$147.8 million for the nine months ended September 30, 2019, which consisted primarily of gross proceeds of \$155.2 million from private placement and public offering of our ordinary shares, which was offset by \$7.4 million in offering costs.

Net cash provided by financing activities was \$130.0 million for the nine months ended September 30, 2018, which consisted of gross proceeds of \$75.0 million from the issuance of ordinary shares in connection with our initial public offering, which was offset by \$9.5 million in offering costs, \$56.9 million from the issuance of our Series C preferred shares, which was offset by \$0.7 million in offering costs, and \$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.

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### ***Funding Requirements***

Our operating expenses have increased substantially in 2019 and 2018 and are expected to increase substantially in the future in connection with our ongoing activities.

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
- continue to 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 on hand and the research funding we expect to receive under the Collaboration and License Agreement, we estimate that we will be able to fund our operating expenses and capital expenditure requirements into 2022. 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 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, 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.

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**Contractual Obligations and Commitments**

There were no material changes in our commitments during the nine months ended September 30, 2019 under contractual obligations as disclosed in our Form 10-K outside the ordinary course of 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, (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.**

There have been no material changes in our market risk from the disclosure included under “Item 7A. Quantitative and Qualitative Disclosures of Market Risk” in the Annual Report on Form 10-K for the fiscal year ended December 31, 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 our Chief 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 concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of September 30, 2019.

**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, 2019 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 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 \$49.3 million and \$61.8 million for the nine months ended September 30, 2019 and September 30, 2018, respectively. As of September 30, 2019, we had an accumulated deficit of approximately \$197.6 million. Since our inception, we have devoted substantially all of our resources to developing our technology platform, establishing our viral vector manufacturing facilities 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, developing our business plans, raising capital, and providing general and administrative support for these operations. We have not yet demonstrated an ability to successfully complete 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 (the “FDA”), European Medicines Agency (the “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.

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.

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### ***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, 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 continue to incur 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, 2019, our cash and cash equivalents were \$253.3 million. Based on our cash and cash equivalents at September 30, 2019 and the research funding we expect to receive under the Collaboration and License Agreement, we estimate that such funds will be sufficient to enable us to fund our operating expenses and capital expenditure requirements into 2022. 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 X-linked retinitis pigmentosa product candidate, AAV-RPGR, for our *CNGB3* achromatopsia gene therapy product candidate, AAV-CNGB3, for our *CNGA3* achromatopsia gene therapy product candidate, AAV-CNGA3, for our *RPE65*-associated retinal dystrophy product candidate, AAV-RPE65, for our radiation induced xerostomia product candidate, AAV-AQP1, and to continue to conduct our ongoing natural history studies for inherited retinal diseases, or IRDs;
- the initiation of Phase 1/2 clinical trials for our product candidate for the treatment of ALS, AAV-UPF1, and for our product candidate for the treatment of xerostomia associated with Sjogren's syndrome, AAV-AQP1;
- future discussions with regulatory agencies and potential subsequent initiation of future clinical trials for our product candidate for the treatment of Parkinson's disease, AAV-GAD;
- 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;
- the cost and timing of completion of commercial-scale manufacturing facilities and activities;
- the cost of making royalty, milestone or other payments under current and any future in-license agreements;
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements;

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- the extent to which we in-license or acquire rights to other products, product candidates 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, 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-RPGR, AAV-CNGB3, AAV-CNGA3, 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-RPGR, AAV-GAD, AAV-CNGB3, AAV-CNGA3, AAV-RPE65 and AAV-AQP1 (the “Most Advanced Product Candidates”), 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 our Most Advanced Product Candidates, which may never occur. We cannot be certain that our Most Advanced Product Candidates 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 our Most Advanced Product Candidates 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 our Most Advanced Product Candidates in the United States until they receive approval of a biologics license application, or BLA, from the FDA, we cannot market them in the European Union until we receive approval for a Marketing Authorization Application, or MAA, from the EMA, and we cannot market them in other countries until we receive any other required regulatory approval in those countries.

AAV-GAD, AAV-RPGR, AAV-CNGB3, AAV-CNGA3, 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 our Most Advanced Product Candidates 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.

***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;

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- 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 may be 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 control 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 two product candidates 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, or IV, 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.

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***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, had historically been subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or the RAC, pursuant to the NIH Guidelines for Research Involving Recombinant DNA Molecules, or NIH Guidelines. Following an initial review, RAC members would make a recommendation as to whether the protocol raised important scientific, safety, medical, ethical or social issues that warranted in-depth discussion at the RAC's quarterly meetings. Although the FDA decides whether individual gene therapy protocols may proceed under an IND, the RAC's recommendations were shared with the FDA and the RAC public review process, if undertaken, could have impeded or delayed the initiation of a clinical trial, even if the FDA had reviewed the trial and approved its initiation or had notified the sponsor that the study may begin. Conversely, the FDA can put an IND on clinical hold even if the RAC provided a favorable review or has recommended against an in-depth, public review.

On August 17, 2018, the NIH issued a notice in the Federal Register and issued a public statement proposing changes to the oversight framework for gene therapy trials, including changes to the applicable NIH Guidelines to modify the roles and responsibilities of the RAC with respect to human clinical trials of gene therapy products, and requesting public comment on its proposed modifications. During the public comment period, which closed on October 16, 2018, the NIH has announced that it will no longer accept new human gene transfer protocols for review as part of the protocol registration process under the existing NIH Guidelines or convene the RAC to review individual clinical protocols. These trials will remain subject to the FDA's oversight and other clinical trial regulations, and oversight at the local level will continue as otherwise set forth in the NIH Guidelines. Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an IBC. The IBC assesses the safety of the research and identifies any potential risk to the public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. Even though we may not be required to submit a protocol for our gene therapy product candidates through the NIH for RAC review, we will still be subject to significant regulatory oversight by the FDA, and in addition to the government regulators, the applicable IBC and institutional review board, or IRB, of each institution at which we or our collaborators conduct clinical trials of our product candidates, or a central IRB if appropriate, would need to review and approve the proposed clinical trial.

In Europe, 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,

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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 is 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 several Phase 1/2 clinical trials and completed dose escalation in two of those 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;

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- 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 our product candidates for use in clinical trials.

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 they 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

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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.

Our most advanced product candidates, AAV-GAD, AAV-RPGR, AAV-CNGB3, AAV-CNGA3, 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 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 Form 10-Q should be viewed with caution. Further, the data and statistical information included, or supporting the information, in this 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 patients' 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,

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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 designated a Fast Track program by the FDA for the treatment of achromatopsia caused by CNGB3 mutations to improve visual function.

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 2 meeting with FDA. If the FDA grants breakthrough therapy designation, it may take actions appropriate to expedite the development and review of the product candidate, 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 I; organizational commitment involving senior managers; and eligibility for rolling review and priority review of a BLA. 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

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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-CNGB3, AAV-CNGA3, 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 EMA for AAV-CNGB3 for the treatment of achromatopsia caused by mutations in the *CNGB3* gene, for AAV-CNGA3 for the treatment of achromatopsia due to autosomal-recessive *CNGA3* gene mutations, for AAV-RPE65 for the treatment of Leber congenital amaurosis, for AAV-RPGR for the treatment of retinitis pigmentosa and for 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. 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

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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 and are in the planning stages of expanding our manufacturing capabilities, including building a second viral vector facility as well as a cGMP plasmid production facility. However, if we experience slowdowns or problems with our completed facility or the construction of our new facilities 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 of 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.

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***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 sites.

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.

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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 and / or our Collaboration and License Agreement partner obtain FDA or EMA approval for AAV-GAD, AAV-RPGR, AAV-CNGB3, AAV-CNGA3, AAV-RPE65 or AAV-AQP1 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.

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;

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- 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. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. 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.

***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:

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- 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;
- 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 & Medicaid 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, Congressional and executive branch challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, the Tax Cuts and Jobs Act of 2017, or the Tax Act, 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". Additionally, on December 14, 2018, a U.S. District Court Judge in Texas ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. While such U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the law. 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 2029 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. On January 31, 2019, the HHS Office of Inspector General proposed modifications to U.S. federal Anti-Kickback Statute safe harbors which, among other things, will affect rebates paid by manufacturers to Medicare Part D plan sponsors, Medicaid managed care organizations, and those entities' pharmacy benefit managers ("PBMs"), the purpose of which is to further reduce the cost of drug products to consumers. 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.

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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.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

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;

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- 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;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- 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 and requirements regarding the collection, distribution, use, security, and storage of personally identifiable information and other data relating to individuals (including the EU General Data Protection Regulation 2016/679, or GDPR).

As of May 25, 2018, the GDPR replaced the Data Protection Directive with respect to the processing of personal data in the European Union. The GDPR imposes many requirements for controllers and processors of personal data, including, for example, higher standards for obtaining consent from individuals if this is required to process their personal data, more robust disclosures to individuals and a strengthened individual data rights regime, shortened timelines for data breach notifications, limitations on retention and secondary use of personal data, increased requirements pertaining to health data and pseudonymised (i.e., key-coded) data and additional obligations when we contract third-party processors in connection with the processing of the personal data. The GDPR allows EU member states to make additional laws and regulations further limiting the processing of genetic, biometric or health data. Failure to comply with the requirements of GDPR and the applicable national data protection laws of the EU member states may result in fines of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, and other administrative penalties.

The U.K. is expected to withdraw from the EU further to a national referendum held on June 23, 2016. The U.K.’s Data Protection Act 2018, or DPA2018, governs the U.K.’s privacy regime and will continue to do so after any withdrawal from EU. The GDPR will form part of U.K. domestic law as “retained EU law” as a result of the EU (Withdrawal) Act 2018, with certain amendments made to it and also to the DPA 2018 and the U.K. Privacy and Electronic Communications (EC Directive) Regulations 2003 under the (draft) Data Protection, Privacy and Electronic Communications (Amendments etc.) (EU Exit) Regulations 2019, which is intended to come into force upon the U.K. withdrawing from the EU. Accordingly, the terms of the GDPR, and its significant penalties, will continue to apply in the U.K. after any withdrawal from the EU. At time of writing, it is unlikely that the U.K. will be granted adequacy by the European Commission (which would allow personal data to flow freely from the EU to the U.K.) before the U.K. withdraws from the EU. The U.K. will become a “third country” upon leaving the EU and data export mechanisms, such as Model Clauses, will need to be put in place to safeguard the transfer of personal data from the EU to the U.K.

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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.

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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, Biogen, Inc. and Spark Therapeutics, Inc, which is being purchased by Roche Holding AG. There are a number of companies developing gene therapy products for neurodegenerative diseases, including Voyager Therapeutics, Inc., Axovant Gene Therapies Ltd. and Preveil Therapeutics Inc. 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

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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;

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- 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-GAD, AAV-RPE65, AAV-AQP1 or other future gene therapy programs, if approved, for the United States 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.

If we are unable to build our own sales force or negotiate a collaborative relationship for the commercialization of AAV-GAD, AAV-RPE65 or AAV-AQP1, we may be forced to delay the potential commercialization of AAV-GAD, AAV-RPE65 or AAV-AQP1 or reduce the scope of our sales or marketing activities for AAV-GAD, AAV-RPE65 or AAV-AQP1. 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-GAD, AAV-RPE65 or AAV-AQP1 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.

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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-GAD, AAV-RPE65 or AAV-AQP1 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-GAD, AAV-RPE65 or AAV-AQP1 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 FCPA, the Bribery Act 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 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 produce our product candidates in our cGMP viral vector manufacturing facility completed in early 2018 and are in the planning stages of expanding our manufacturing capabilities, including building a second viral vector facility as well as a cGMP plasmid production facility. However, if our current facility is damaged, suffers any form of delay or regulatory challenges, we experience slowdowns or problems with the construction of our new facilities 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;

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- 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, and the National Institute of Dental and Craniofacial Research, or NIDCR, a division of the NIH. We are a party to agreements with UCLB for certain technology and AAV vector-related patents and with Brandeis for certain preclinical technology for the treatment of ALS. Further, we are party to an agreement with NIDCR for technology relating to the treatment of Sjogren's syndrome. 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 UCLB, we are obligated to pay an annual management fee, milestone payments for certain commercial sales thresholds, and royalties. If we fail to comply with our obligations to UCLB, Brandeis, NIDCR, 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 proceedings 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. 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.

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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

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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.

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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.

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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.

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***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;
- 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

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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 United States. 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.

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***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, 2019, we had 130 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 Chief Financial 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.

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***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;
- 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.

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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 continuing to operate 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 and our systems and those of our contractors and consultants may be vulnerable to cybersecurity risks.***

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.

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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. Increased cybersecurity threats pose a risk to this information, in addition to our and our contractors' and consultants' systems and networks. Despite our security measures, our information technology and infrastructure may be vulnerable to cyber-attacks by hackers or internal bad actors, or breached due to employee error, a technical vulnerability, malfeasance or other disruptions that could have a negative impact, including loss or destruction of data (including confidential information). Although, to our knowledge, we have not experienced any such material security breach to date, we may experience cybersecurity incidents such as malware infections, phishing attempts, thefts of personal, confidential or proprietary information and other attempts at compromising our information technology that are typical for a company of our size in our market. Any security 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, result in significant expenses in implementing future security measures and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and financial results, 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 terms of any withdrawal are subject to a complex and ongoing negotiation between the United Kingdom and the European Union whose result and timing remain unclear and which has created significant political and economic uncertainty about the future trading relationship between the United Kingdom and the European Union in the event of a withdrawal, particularly in light of the possibility that an immediate, so-called "no deal" withdrawal could occur without a negotiated agreement. 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; tax and customs laws, intellectual property rights; environmental, health, and safety laws and regulations; immigration laws; employment laws; and transport laws, could decrease foreign direct investment in the United Kingdom, increase costs, disrupt supply chains, depress economic activity, and restrict our access to capital. If the United Kingdom and the European Union are unable to negotiate mutually 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 have been and may continue to be especially subject to increased market volatility. In addition, changes to U.K. border and immigration policy could occur as a result of any withdrawal, 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. This transition has caused, and may continue to 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.

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### ***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;
- changes in accounting principles; and
- the other factors described in this “Item 1A. Risk Factors” section and elsewhere in this 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

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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, 2019, 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 62.2% 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, 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.

All lock-up agreements entered into in connection with our IPO expired on December 5, 2018. Subject to any applicable lockup agreement described below, our outstanding ordinary shares may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act, or to the extent that such shares have already been registered under the Securities Act and are held by non-affiliates of ours. Moreover, certain holders of ordinary shares have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their ordinary 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 also have registered all ordinary shares that we may issue under our equity compensation plans or that are issuable upon exercise of outstanding options. Upon issuance, these ordinary shares can be freely sold in the public market, subject to volume limitations applicable to affiliates and any applicable 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 a “smaller reporting company,” and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting 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 (“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 Form 10-Q;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- 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;

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- 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.

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 are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non-voting common shares held by non-affiliates is more than \$250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than \$100 million during the most recently completed fiscal year and our voting and non-voting common shares held by non-affiliates is more than \$700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure, are exempt from the auditor attestation requirements of Section 404, and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors.

We may choose to take advantage of some, but not all, of the available exemptions for emerging growth companies and smaller reporting companies. 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 shares price may be more volatile.

***We will continue to 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 and smaller reporting company, we will continue to 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 Global Select 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 need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and 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 are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we 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.

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***If securities or industry analysts cease to 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 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 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 are also 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 IPO 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,

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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 are 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 Cayman Islands law, we may only make distributions by way of dividend out of profits, or out of our share premium account (provided that immediately following the date that the dividend is proposed to be paid we are able to pay our 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. See the “Dividend Policy” section of the Form 10-K for the year ended December 31, 2018 for additional information.

***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.***

Our board of directors conducts 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, 2018, 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, 2018 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 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.

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### ***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 of our ordinary shares 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 of our ordinary shares should consult their tax advisors regarding the potential application of these rules to their investment 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.

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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 Reorganization Transactions 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 December 31, 2018, we had federal and state NOL carryforwards in the United States of \$14.2 million and \$14.2 million, respectively, and cumulative carryforward tax losses in the United Kingdom of \$94.1 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 carryforwards incurred prior to January 1, 2018 in the amount of approximately \$6.8 million and \$6.7 million will begin to expire in 2036. The U.K. carryforward tax losses will continue indefinitely, subject to relevant restrictions, under current UK legislation. Under the Tax Act, U.S. federal NOL carryforwards generated after December 31, 2017 are not subject to expiration but such NOLs may only offset 80% of taxable income. As of December 31, 2018, we also had orphan drug and research and development credits in the U.S. in the amount of \$1.1 million.

The NOL carryforwards 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. We have conducted a review of changes in the ownership interest of significant shareholders and determined that as of December 31, 2018, there were no limitations in the U.K. However, for U.S. purposes, we have determined that a change of ownership occurred in April 2016. We are still in the process of determining the annual limitation on losses that occurred prior to April 2016. 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 and orphan drug credits. As such, the U.S. research and development and orphan drug 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.**

None.

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

None.

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**Item 4. Mine Safety Disclosures.**

Not applicable.

**Item 5. Other Information.**

None.

**Item 6. Exhibits.**

<b>Exhibit Number</b>	<b>Description</b>	<b>Form</b>	<b>File No.</b>	<b>Exhibit</b>	<b>Filing Date</b>	<b>Filed/Furnished Herewith</b>
31.1	<a href="#"><u>Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u></a>					*
31.2	<a href="#"><u>Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u></a>					*
32.1	<a href="#"><u>Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u></a>					**
32.2	<a href="#"><u>Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u></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.



## CERTIFICATION

I, Alexandria Forbes, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2019 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) [intentionally 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 7, 2019

By: \_\_\_\_\_  
*/s/ Alexandria Forbes*  
**Alexandria Forbes**  
**President and Chief Executive Officer**  
*(principal executive officer)*

## CERTIFICATION

I, Richard Giroux, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2019 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) [intentionally 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 7, 2019

By: \_\_\_\_\_  
/s/ Richard Giroux  
**Richard Giroux**  
**Chief Financial Officer and Chief Operating 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 Form10-Q for the quarterly period ended September 30, 2019 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 to the best of my knowledge:

- (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 results of operations of the Company.

Date: November 7, 2019

By: \_\_\_\_\_ /s/ Alexandria Forbes  
**Alexandria Forbes**  
**President and Chief Executive Officer**  
*(principal executive officer)*

